MANAGEMENT *of* PAIN *in* CANCER

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Preface

THE AIM of this book is to guide the family physician in his efforts to mitigate the agonies of terminal malignancy We have accordingly marshaled descriptions of all the pain relieving procedures that we have found useful in our own experience The most common approach–the use of analgetic drugs–is presented first in the hope of providing some helpful methods of using the familiar agents as well as the newer synthetic analgetics and opiate antagonists The subsequent chapters present descriptions of clinical procedures to help the general practitioner achieve technical competence in their performance or have a better understanding of the contributions that can be made by experts in specialized fields of medicine and surgery We have sought to give expression to differences of opinion regarding the use of these procedures in order to provide a clear appreciation of the problems relating to the management of terminal malignancy In recognition of the fact that it is not the patient alone who suffers, we have also concerned ourselves to some extent with the reactions of the family and the attending physician

We have tried to provide information regarding means of alleviating the misery and sorrow as well as the pain that closes the cancer episode

We are indebted to Dr Harry Beckman for suggesting the preparation of this book and for his most valuable criticism and encouragement We owe heartfelt thanks also to our colleagues for their generous assistance and advice The publisher contributed more than skilled technical assistance the confidence and co operation of his staff during the preparation of the book lightened our task immeasurably

Foreword

THIS VOLUME deals with a subject neglected far too much by the medical profession and accordingly serves an important function by contributing to the scant knowledge in this field The large number of persons developing cancer and the many who have severe pain in the terminal stage of the uncured disease make the subject of vital importance

In the seven chapters constituting this volume the authors discuss numerous phases of the treatment of pain including analgetics nerve blocks neurosurgical aspects chemotherapy surgical procedures radiation and psychogenic aspects The inclusion of these several mechanisms indicates that no single one will be efficacious in all patients and emphasizes the necessity of utilizing all possible methods in controlling pain

Unfortunately practically all the drugs that are really effective in controlling pain are habit producing and therefore must be used sparingly Nerve blocks which are very important in therapy because they are reasonably effective and can be done without an operation require great skill in injecting the anes

thetic agent into the right areas and in proper amounts Regardless of the type of therapy used there is a tendency to blame a poor result on the "neurotic condition" of the patient and this situation allows the patient to slide rapidly into drug addiction We must appreciate that severe constant pain of the type commonly present in terminal cancer will destroy the morale of the sturdiest individual Moreover the devastating effect of severe pain will make the patient particularly susceptible to the various discomforts present in terminal cancer and thus lower his pain threshold The physician must recognize these conflicting factors and accept them as part of his responsibility rather than neglect the patient because he may be developing a neurotic tendency

On many occasions the terminal phase progresses so rapidly that there is not enough time between onset of the severe pain and death for addiction to a narcotic to become very important and under such conditions analgetic treatment fills the need quite satisfactorily But since it is extremely difficult—in fact impossible—to predict duration of life with cancer we are often loathe to give liberal amounts of narcotics because the drug addiction itself may become a hideous spectacle and actually result in great misery for the patient

In their discussion of therapeutic measures the authors have appropriately included operative procedures of a palliative nature This is an important aspect of therapy in a patient with terminal cancer because relief from one discomfort or pain may make the remaining one or others bearable As is emphasized in

Chapter V, the indications for these palliative procedures are by no means clear For example it is well known that resection of a carcinoma of the rectum or colon is desirable even though there may be metastases in the liver that removal of the ulcerating tumor mass eliminates the loss of blood and serum from the ulcer and likewise minimizes terminal pain which is usually very severe in patients who do not have the rectal lesion excised However good judgment is necessary in choosing the patients, since an unsuccessful attempt to remove the involved bowel might make the tumor grow much more rapidly—if for instance tumor tissue was cut across during the operation

For reasons presented here and in the text, we must take advantage of all possible measures to reduce the discomfort and pain of terminal cancer The authors are to be congratulated for having covered these various points in an admirable fashion and for having devoted the proper attention to the details of the various types of therapy

—WARREN H COLE

Table of Contents

CHAPTER 1

Systemic Analgetics

GENERAL CONSIDERATIONS

THE USE OF any systemic analgetic should be considered in relation to a number of factors such as the degree of pain the clinical condition of the patient the immediate prognosis the proposed therapy and the probability of its success life expectancy and the ability of the patient to carry on a normal role in society The prognosis in malignancy is not necessarily related to the degree of pain For example prostatic carcinoma with extensive metastases may have a negative prognosis yet the pain from the metastatic involvement may be so slight as to be controlled by aspirin The choice of analgetic therefore should rest primarily on the degree of pain Most pain situations are acute and analgetics are consequently used as a temporary device pending direct attack on the cause of pain In the presence of malignancy however the effectiveness of surgery chemotherapy and radiation is often in doubt and the physician must be prepared to provide for relief of chronic rather than acute pain

The life expectancy will influence the choice of

agents used For example if the prognosis indicates a terminal course that can be measured in weeks every effort should be made to provide relief of pain regardless of such considerations as addiction The medical and social problems of addiction are unimportant when the few remaining days of life need the blessed relief provided by the opiates This is important not only to the patient but to the members of his family who suffer with him Addiction and particularly tolerance are important in the patient with long term chronic pain In such instances every effort should be made to put off the use of the potent addicting drugs until all other measures have been exhausted The patient may have a year or more of life important to himself, his family and society The analgetics used in such circumstances should provide adequate pain relief with a minimum of interference with his normal functions and behavior Whenever possible in such conditions nonaddicting drugs should be used If these prove inadequate, codeine is the drug of choice because of its relatively low addiction potential If opiates or opioids must be used, oral medication is preferred It is important to inform the family of the characteristic effects of the opiates (such as tolerance addiction and nausea) so that they can make a satisfactory adjustment to the patient s subsequent behavior and symptoms

The fear of intolerable pain is best overcome by conditioning the patient to expect relief after administration of the analgetic This can be achieved by in

suring the adequacy of the dose and by giving the drug promptly on the appearance of pain Pain itself is a most potent antagonist not only to the untoward effects of the analgetics but to the analgesia itself Therefore full doses should be given when the pain is moderate instead of waiting until the patient writhes in pain The fear of pain and the individual reaction to pain can also be modified by the use of agents other than the analgetics such as barbiturates am phetamine and other drugs that affect the emotional plane and sensorium

NONADDICTING DRUGS

The salicylates paraminophenols and pyrazolones (as exemplified by aspirin phenacetin and antipyrine respectively) are nonaddicting drugs with moderate analgetic effect They are of little or no value in deep visceral pain Combinations of this group of agents with barbiturates, sympathomimetics caffeine or co deine are useful and often may be employed to greater advantage than the individual components used singly The continued use of these agents for chronic pain carries the risk of increased possibility of toxic re actions

Cinchonism or salicylism following the use of sali cylates resembles quinine intoxication Visual and auditory disturbances tachycardia hyperpnea central excitation and lowered prothrombin values are among the signs of salicylate intoxication Severe salicylate toxicity can produce dyspnea central nervous system

depression renal dysfunction and respiratory failure Although the paraminophenols (for example phenacetin) are not addicting agents they are habit forming The signs of chronic toxicity are sometimes easily confused with symptoms arising from the patient s primary disease Among these indications of paraminophenol toxicity are cyanosis a typical bluish color of the mucous membranes anorexia secondary anemia leukocytosis jaundice and oliguria The pyrazolones (antipyrine for instance) may produce toxicity resembling that of the paraminophenols with the exceptions that cyanosis and methemoglobinemia are not characteristic Antipyrine toxicity is commonly indicated by pink to purple macular patches, whereas the use of aminopyrine is accompanied by the danger of agranulocytosis

ADDICTING DRUGS

At least two considerations must be understood and appreciated in order to provide for the intelligent choice and use of the addicting analgetics They are tolerance and analgetic intensity

Tolerance for practical purposes in the management of pain in malignancy can be defined as that characteristic which requires increasingly larger doses to provide the same effect as was produced by the original dose For example 10 mg (1/6 gr) morphine may be an adequate dose in a hypothetical case but as the drug is used regularly over a period of time it no longer proves effective and 30 mg (1/2 gr) may be

needed to give the same pain relief that was originally produced by one third that amount of morphine Tolerance to addicting drugs begins early, in fact there is good evidence that it is operative after the very first dose Factors facilitating the development of tolerance include the administration of the drug at frequent regular intervals and the use of successively larger doses The appearance of clinically significant tolerance can be delayed by using the minimal effective dose as infrequently as possible and by limiting the use of addicting drugs to their primary characteristic analgesia and not to secondary properties such as sedation The writing of such an order as "¼ gr morphine q 4 h" is to be deplored Addicting analgetics are to be ordered on the basis of pain, not according to the clock or nursing habits Unfortunately cross tolerance exists among the potent analgetics This means that if tolerance has developed to morphine it will also operate with similar drugs For example using the hypothetical case referred to above, when 10 mg morphine was first used it was probably interchangeable with about 2 mg levorphan After the development of tolerance at which time the morphine requirement was increased threefold more than 2 mg of levorphan would be needed if it were desirable to change to this drug Thus one cannot change opiates without making allowance for the effects of tolerance The need for increasingly larger doses may proceed to the point where pain relief becomes an economic burden

The maximum analgetic intensity is a property pe-

culiar to each of the potent analgetics For every such drug there is a correlation between the dose and the intensity of analgesia *within certain limits* It is the limit of this relationship with which we are concerned For example the maximum analgetic intensity (maximum increase in pain threshold) of codeine is achieved with about 65 mg (1 gr) Therefore, in a given case of acute pain if this dose of codeine does not provide relief, little advantage is obtained from larger doses The characteristic maximum analgetic intensity can be expressed in another fashion every potent analgetic has a dose beyond which increments in dosage produce increasingly smaller increments in the intensity of analgesia Examples of these critical doses are meperidine 150 mg and morphine 30 mg (½ gr)

The degree of maximum intensity of analgesia is usually measured as the maximum per cent increase in pain threshold Some maximums are codeine, 50 per cent meperidine 60 per cent and very large doses of morphine approximating 100 per cent Dihydromorphinone and levorphan are examples of drugs which readily provide increases of 100 per cent The clinical significance of these figures is that pain which does not respond to codeine is unlikely to be affected materially by meperidine On the other hand, where large doses of morphine prove unsatisfactory good analgesia may be obtained with such drugs as dihydromorphinone or levorphan

The toxicity of the addicting analgetics is sufficiently well known to require no elaborate exposition here Attention might, however be invited to a few basic

considerations sometimes overlooked The morphine like drugs are depressant except in their action on the vomiting center the lower sections of the spinal cord and the gastrointestinal tract where they are primarily excitatory The effects on the gastrointestinal tract include delayed gastric emptying time and constipation It is surprising how often the former is forgotten and patients are given oral medication shortly after administration of an opiate Since there is considerable variation in the individual response to any opiate, it is often advantageous to rotate the drugs being used in order to achieve maximum effectiveness with a minimum of untoward reactions

The cause of death from opiate intoxication is respiratory failure Severe opiate-induced respiratory depression is treated specifically by the intravenous administration of nalorphine (Nalline 5 mg) or levallorphan (1 mg) These drugs should be given until the desired respiratory response is obtained Overdosage should be avoided since these narcotic antagonists have depressant effects and, when given to excess will themselves produce respiratory depression Patients requiring treatment with such agents should be observed closely for at least 24 hours The antagonists will reverse or inhibit all the pharmacologic effects of the opiates including respiratory depression *and analgesia* When given to an addict the narcotic antagonists will provoke violent abstinence symptoms

An interesting use of the antagonists is to combine them with an opiate in order to permit administration of a larger dose of the analgetic without increased risk

of respiratory depression Cullen and Santos (A M A Arch of Surg 69 410 1954) used a combination of 5 mg levorphan and 0.5 mg levallorphan to obtain analgesia without respiratory depression in patients with chronic pain Not all of the narcotic analgetics have been studied as yet regarding the specific ratio of opiate to antagonist

Included among the opiates are such drugs as codeine dihydrocodeinone morphine 6 methyldihydromorphinone and dihydromorphinone The opioids are synthetic addicting analgetics such as meperidine methadone alphaprodine and levorphan All agents in this group are subject to the Harrison Narcotic Act Their general characteristics dosage forms and routes of administration are listed below The suggested doses are those which will produce approximately the same rise in pain threshold as 10 mg (⅙ gr) morphine sulfate

Codeine

Codeine is available as the free base or in the form of water soluble phosphate or sulfate salts Pharmacologically it resembles morphine except as listed below Codeine is an addicting drug but its addiction potential is less than that of any of the other opiates It will produce a maximum increase in pain threshold approximately half as great as that of morphine These two factors serve to make codeine the drug of choice for moderate visceral pain If a nonaddicting agent is incapable of providing satisfactory analgesia and an opiate must be used codeine should be tried before

the more potent and more addiction liable drugs Codeine although it will produce constipation generally provokes fewer unfavorable reactions than equivalent doses of morphine It has a shorter duration of action and produces less euphoria sedation and respiratory depression than morphine Toxic doses of codeine lead to excitation rather than depression The analgesia of codeine also differs from that of morphine in that codeine does not produce indifference to pain Morphine and the other potent drugs affect the patient s reaction to pain in such a fashion that, although the patient recognizes the pain he often says "It feels as though it s happening to someone else"

Although combinations of codeine with salicylates caffeine etc are often used to advantage, the maximum effect of codeine is not attained when the drug is given orally When pain results from a condition such as malignancy it is advisable to give codeine subcutaneously in order to achieve the maximum analgetic effect Because codeine is not commonly used by opiate addicts the erroneous impression persists that it is not an addicting drug Its continued use however will produce tolerance and the entire sequence of addiction Thus, physical dependence gastrointestinal disturbances emaciation etc are consequences of the continued use of codeine The most effective dose is 65 mg (1 gr) either subcutaneously or intravenously There is no advantage in the use of larger doses save in the presence of tolerance The maximum analgetic effect is reached 30-60 minutes after subcutaneous injection

Dihydrocodeinone

Dihydrocodeinone (Hycodan, Dicodid) has the same chemical relationship to dihydromorphinone (Dilaudid) as codeine has to morphine It is more potent than codeine on a weight basis and has a greater addiction potential but otherwise differs little from codeine The usual oral dose of the bitartrate salt is 10 mg

Morphine

Morphine is the classic opiate for the relief of severe pain and is the standard against which all the other potent analgetics are measured Given orally, it produces little analgesia and therefore the parenteral routes are preferred In the presence of acute overwhelming pain morphine may be given intravenously since this method provides the quickest and most intense analgesia When morphine is given subcutaneously the maximum analgetic effect is obtained in 60–90 minutes This analgesia is not so intense as that provided by intravenous administration but it is more prolonged There are diminishing returns when doses larger than 10 mg (¼ gr) are used in the absence of tolerance Indeed, if this dose of morphine does not give adequate control of pain it may be advantageous to change at once to those drugs which will easily provide a 100 per cent increase in the pain threshold Although larger doses of morphine are often used the resulting analgesia is accompanied by an increase

in the number and severity of undesirable reactions Among the most common of such reactions are nausea emesis vertigo miosis hypnosis respiratory depression constipation pruritus oliguria and ur ticaria

Morphine often produces a sense of well being be yond what might be expected to occur on the basis of the reaction to the relief of pain This sense of well being is a desirable effect because the patient is comfortable and co operative If pain is still perceived the patient is indifferent to it This alteration in the *reaction to pain* is one of the most valuable char acteristics of morphine and the other potent analgetics The patient is aware of pain but he feels that it is no longer part of him He recognizes it as he would an impersonal object in the room and since his thoughts are no longer completely centered on pain he can think and act in a rational manner The picture is completely different when euphoria results from the administration of a drug such as morphine then the patient is definitely unco operative and his thoughts are turned inward as he experiences a sense of ex hilration and exaltation There are great differences in the individual responses to morphine some patients experience a sense of well being others euphoria The reactions of any one patient to morphine are not neces sarily the same as those which would be obtained if another opiate were used The patient s response to euphoria will, to a great extent be a reflection of his basic psychologic characteristics To some individuals

this change in emotional plane will be more significant than any alteration of pain and the patient s demands for morphine will warn of the impending danger of addiction It therefore becomes increasingly important to make certain that morphine be given for its primary indication—pain—rather than for a change in mood or emotional status

Since the liver plays an important role in the detoxification of morphine the drug will often produce exaggerated effects when given to a patient with hepatic disease Morphine increases the cerebrospinal fluid pressure and this prevents its use when intra cranial pressure is already increased Among other conditions which contraindicate the use of morphine are pruritus myxedema acute renal damage and bronchial asthma

Dihydromorphinone

Dihydromorphinone (Dilaudid Hymorphan) is the most potent of the opiates on a weight basis Since it is more effective orally than is morphine 2–3 mg is given by this route The subcutaneous dose is usu ally 2 mg Although dihydromorphinone will produce a 100 per cent increase in the pain threshold it has a shorter duration of action than morphine Rectal suppositories containing 2 5 mg of the hydrochloride salt are used in an attempt to delay absorption of the drug and thus provide a longer duration of the anal getic effect Dihydromorphinone is an addicting drug and the frequency with which it must be given for

chronic pain constitutes a serious disadvantage The other pharmacologic effects of dihydromorphinone are similar to those of morphine with the following exceptions reactions such as nausea emesis and constipation are less severe and frequent, and sedation is not so marked as with morphine an advantage when a hypnotic effect is undesirable The euphorogenic properties of dihydromorphinone are less than those of morphine

6 METHYLDIHYDROMORPHINONE

6 Methyldihydromorphinone (Metopon) is the methyl derivative of dihydromorphinone and has some of the parent compound s characteristics It is more effective than morphine when given orally The only dosage form commercially available is a 3 mg capsule Reactions such as nausea, emesis and constipation occur less frequently than with morphine and the hypnotic and euphorogenic effects are also less This drug has an advantage over dihydromorphinone in that the duration of the analgetic effect is approximately the same as that of morphine Although 6 methyldihydromorphinone is an addicting drug it appears that tolerance develops relatively slowly and that there is a comparatively rapid dissipation of the abstinence syndrome when the drug is withdrawn These considerations however do not alter the necessity for taking the same precautions that apply to any addicting agent According to N N R (1955) the drug is recommended only for severe persistent pain

Meperidine

Meperidine (Demerol Pethidine isonipecaine) was the first successful synthetic substitute for morphine Its pharmacologic properties which are related to morphine codeine and atropine make meperidine a useful drug for the relief of moderate visceral pain The usual dose is 50–100 mg orally or by intramuscular injection The increase in pain threshold following the intramuscular administration of 100 mg meperidine is approximately the same as that of 10 mg (⅙ gr) morphine In the absence of tolerance there is little to be gained from doses greater than 150 mg One of the most important factors limiting the use of this drug is that it cannot provide much more than a 60 per cent increase in pain threshold This means that if full doses (65 mg 1 gr) of codeine have been given without obtaining adequate control of pain in all probability meperidine will also fail

The undesirable reactions to meperidine are vertigo nausea emesis mydriasis and tachycardia The fre quency of vertigo limits the use of this drug in am bulatory patients Neither a sense of well being nor euphoria is a characteristic consequence of the use of meperidine Unlike most other opiates and opioids described in this chapter meperidine intoxication pro duces excitation rather than depression Meperidine has a wide margin of safety, but large toxic doses may provoke twitching muscular inco ordination disori entation and convulsions If the dose is very excessive

the period of excitement is followed by respiratory depression coma and death

The contraindications to the use of meperidine include increased intracranial pressure and severe hepatic disease Since meperidine is an addicting drug the usual precautions for such agents apply to its use

Methadone

Methadone (Adanon Dolophine Methadon) was synthesized in Germany about the time of World War II Its advantages over morphine include oral effectiveness and the ability to provide a 100 per cent increase in pain threshold The usual dose is 10 mg, orally, but sometimes subcutaneously or intramuscularly According to N N R (1955) the intravenous route should not be used Since methadone produces local irritating effects the oral route is preferred but if parenteral administration must be used the size of the dose should be held to a minimum The oral effectiveness of methadone its analgetic potency and the lack of marked sedative effects help to make it a desirable drug in the management of chronic pain

Vertigo nausea and emesis are the most common undesirable effects attending the use of methadone Euphoria rarely occurs The depressive toxic effects of large doses are similar to those of morphine Although methadone is an addicting agent the abstinence syndrome following its withdrawal is much less severe although more prolonged than that of morphine This moderation of the abstinence syndrome

does not warrant indiscriminate use of the drug it should be used with the same caution as any other addicting agent

Alphaprodine

Alphaprodine (Nisentil prisilidene Nu 1196) was synthesized by Ziering and Lee in 1947 Although less potent than morphine on a weight basis alphaprodine has significant advantages over morphine It is equally effective orally or by any parenteral route and it readily gives rise to a 100 per cent increase in pain threshold The onset of the analgetic effect is very rapid and usually occurs within five minutes after subcutaneous administration It is therefore not necessary to use intravenous or intramuscular injection for a rapid effect The duration of effective analgesia is about one hour following a subcutaneous dose of 20 mg This dose will produce approximately the same rise in pain threshold as will 10 mg (⅙ gr) morphine Larger doses of alphaprodine will increase the intensity and duration of analgesia Doses of 40–60 mg are frequently used in obstetrics Just as the analgetic effects of meperidine resemble those of codeine so the analgesia produced by alphaprodine is in many ways similar to that of dihydromorphinone Although alphaprodine has been used most extensively for acute pain in obstetrics urology and orthopedics suitable doses provide the duration and intensity of analgesia needed for the control of any chronic pain The flexibility of the drug over a relatively wide dosage range makes it adaptable to most pain problems

The undesirable reactions to alphaprodine are, in general, the same as those to morphine except that respiratory depression is not as marked following the use of alphaprodine It is an addicting drug and therefore the dose should be large enough to reduce the frequency of its administration for chronic pain

Levorphan

Levorphan (Levo Dromoran) is the levo optical isomer of 3 hydroxy N methylmorphinan tartrate It is the most potent of the opioids on a weight basis The subcutaneous injection of 2 mg produces an analgetic effect equal to that of 10 mg (⅙ gr) morphine and readily gives rise to a 100 per cent increase in the pain threshold It is equally effective by any route of administration Levorphan differs from morphine in that it has a longer duration of effect and constipation occurs infrequently Experimental data in animals indicate that although the depth of respiratory depression is the same with both levorphan and morphine the duration of the depression is less with levorphan The other pharmacologic effects of levorphan are much the same as those of morphine The properties and characteristics of levorphan make it a useful drug for the most severe chronic pain

Levorphan is an addicting agent and has no advantage over the other drugs in this respect The contraindications and precautions attending its use are the same as those for morphine

Abstinence Syndrome

The abstinence (withdrawal) syndrome appear when an opiate or opioid is abruptly discontinued after the development of addiction The syndrome consists of an unmasking of excitatory phenomena These have been described and measured by Himmelsbach The symptoms vary in intensity and clinical significance Among the milder and more moderate symptoms are yawning lacrimation perspiration tremors anorexia and dilated pupils More unpleasant and serious manifestations are fever insomnia emesis diarrhea and loss of weight

Although the management of the abstinence syndrome is beyond the usual province of the general physician there are rare occasions when he is faced with this problem as the result of definitive therapy in malignancy Obviously the best treatment is to prevent addiction In actual practice however the best that can be done is to delay or diminish the emergence of tolerance as previously described Bifrontal leukotomy (Chap III) will affect the abstinence syndrome The narcotic antagonists (nalorphine and levallorphan) are of no value indeed, if they are given to an addict, they will provoke violent symptoms of abstinence The clinical management of the syndrome is a highly specialized technic and reference should be made to the publications of Eddy Isbell, Wikler and Fraser of the U S Public Health Service In general a course consisting of rapid transference to drugs

which produce less severe abstinence is followed For example if the patient is addicted to morphine methadone is first substituted, and it in turn may be followed by substitution with codeine The general rule is to reduce the frequency, dose and potency of the drugs as rapidly as clinical considerations permit, at the same time providing symptomatic relief by the use of *nonaddicting* agents

ADJUNCTS AND MISCELLANEOUS AGENTS

SEDATIVES

Sedation can be an important and useful adjunct in the management of pain It is especially valuable in diminishing the fear of pain and altering the reaction to pain With proper sedation it is often possible to reduce both the dose and the frequency of opiate administration Although respiratory depression is not common after the usual sedative dose it must be remembered that the depressant effects of a barbiturate and an opiate are additive There are many barbiturates with different characteristics, from which the physician can make his selection A nonbarbiturate sedative, such as methyprylon (Noludar), can be used to advantage in doses of 50–100 mg t i d If sedatives are administered orally they should be given before opiate medication because of the delayed gastric emptying time that is produced by the narcotic analgetics The barbiturates and other drugs may be em

ployed usefully for hypnosis Narcotics should not be used to obtain a secondary effect such as sedation

Chlorpromazine

Chlorpromazine (Thorazine) has many applications in the management of malignancy It has sedative but not hypnotic properties it is a potent antiemetic and as such is useful with radiation or nitrogen mustard therapy and it can reduce the requirements for opiates The usual oral dose to provide for a reduction in narcotics is 25 mg b i d or 10 mg t i d but the drug can also be administered by slow and deep intramuscular injection It is important to reduce the narcotic dose as soon as chlorpromazine treatment is begun A useful schedule is to give one half the usual dose of the opiate until the patient s response to the combined drugs can be evaluated, in some cases the narcotic requirement can be reduced to one quarter the original dose Maintenance dosage of chlorpromazine and the opiate is determined by the patient s response

Chlorpromazine should not be used in patients who have received large or unknown quantities of opiates barbiturates or alcohol, and the occasional hypotensive effects of the drug may make its use undesirable in the presence of arteriosclerosis or cardiovascular disease The sedative and hypotensive effects of chlorpromazine limit its use in ambulatory patients The physician should be on the alert for signs of jaundice

which has been reported to occur following the administration of chlorpromazine

Cobra Venom

The mechanism by which cobra venom produces analgesia is uncertain Although the literature contains favorable reports on its effectiveness, this drug has not received the wide acceptance that one might expect for a non narcotic agent. Cobra (Naja) venom solution is marketed in ampules containing 10 mouse units per ml The usual dosage schedule is 2 5 units intramuscularly the first day and 5–10 units each succeeding day for one week Since the analgetic action is delayed the drug should be used for one week before evaluating its effect If the opiate dose cannot be reduced by that time, or if there is no evidence of analgetic effect, there is little to be gained by continuing the drug If the cobra venom is effective 5–10 units 2–3 times a week will provide for maintenance of the analgetic effect The usual reactions to cobra venom are nausea emesis diarrhea and pain at the site of the injection

CHAPTER 2

Nerve Blocks for Pain in Malignancy

THE INTRACTABLE PAIN that may develop with carcinoma not only vexes but frequently taxes the resourcefulness of the physician The analgetic drugs are usually resorted to but invariably, a point of diminishing returns is reached Drugs may literally be poured into a patient without producing the hoped for relief An answer to this problem of pain may be found in nerve blocks It is not the perfect answer, yet it may mitigate a seemingly hopeless situation

PRINCIPLES OF NERVE BLOCKING

When performing blocks it will be well for the operator to know the principles essential to the proper execution of a nerve block for pain in carcinoma or of nerve blocks in general He should have

1 An understanding of pain mechanisms in carcinoma
2 A knowledge of the anatomy of pain pathways

3 Familiarity with block technics and blocking agents
4 Special instruments or procedures that will help increase or evaluate the success of a block
5 Patience

1 An understanding of the *mechanisms* or pathologic physiology of pain in carcinoma is necessary for the successful prosecution of an effective nerve block These mechanisms are quite varied If a hollow viscus is involved eventual obstruction with consequent *distention* will cause pain In addition the distention can cause obstruction to the blood supply of the area involved giving rise to local hypoxia and more pain Such pain perpetuates itself by causing reflex vasoconstriction—vasoconstrictor impulses propagated along the efferent sympathetic arm of the autonomic nervous system Interestingly enough visceral pain impulses which are normally somatic are conveyed by nerve fibers that travel with the sympathetic nervous system The neuron is found in the dorsal root ganglion If on the other hand a solid viscus is involved, distention of its capsule or serosa may or may not cause any pain As the tumor grows it encroaches on contiguous areas and may provoke pain in many different ways It may by its mass exert *pressure on adjacent viscera* and cause pain It may *invade nerve roots and other nerve structures* It may *invade blood vessels and erode them* It may *cause obstruction of blood vessels to a distal structure* and produce hypoxia and pain It may *invade periosteum and bone, even to the extent of fracture* The fractured bone may in

turn affect nerve roots or other nervous structures The tumor may grow into joints and their capsules giving rise to an arthritis like pain Finally, it may metastasize and produce pain distant to the principal site but necessarily following the patterns mentioned above

2 A knowledge of the peripheral arm of the perception pathways and their points of accessibility is necessary for the effective performance of blocks Briefly pain sensation as perceived by receptors in various organs and structures of the body travels along well defined nerve pathways These are either the peripheral mixed somatic nerves or the autonomic nerve plexuses An outstanding fact which must be appreciated is that all nerve structures conveying pain have their primary neuron in the dorsal root ganglion The somatic nerves may thus be blocked along their course—that is by means of an intercostal paravertebral epidural or spinal nerve block The cranial nerves and the autonomic ganglia associated with them may best be approached at their points of exit from the various foramina of the skull The autonomic nerve plexuses may be attacked in the prevertebral area (for example splanchnic block) or in the paravertebral areas—lumbar thoracic or cervical

3 Skill and familiarity with the block technic increase the success of the procedure Although skill may be considered essential lack of it should not be construed as a deterrent to the uninitiated since skill in this field may be acquired by frequent actual performance under good supervision Familiarity and skill imply an adequate knowledge of the anatomic loca

tion of the nerve or plexus to be blocked and the utilization of bony landmarks which can help greatly in the proper placement of a block needle Familiarity and skill also assure the proper positioning of the patient In the improperly positioned patient, important landmarks may be obscured and the accessibility of a nerve may be diminished Familiarity also implies the availability of equipment in excellent working condition The use of needles with snagged or dull points is an unconscionable practice which is to be deprecated

4 Certain special procedures can help evaluate or increase the success of a block The simplest proof of whether a nerve block is effective or not lies in the relief of pain in the area of distribution of the nerve and the development of parasthesia or analgesia in the same site This is true of somatic nerves One must remain aware, however of the fact that fear and apprehension occasionally provoke an alarm reaction which develops a state of numbness or analgesia in the patient Such a condition may be misleading in the interpretation of the outcome of a block The blocking of any portion of the sympathetic nervous system may give rise to definite syndromes An outstanding example of this is Horner s syndrome which develops after a stellate ganglion block it usually consists of miosis relative enophthalmos ptosis conjunctival injection dryness of the face and stuffiness of the nostril on the ipsilateral side The determination of skin temperatures before and after a block of sympathetic ganglia especially if compared with the op

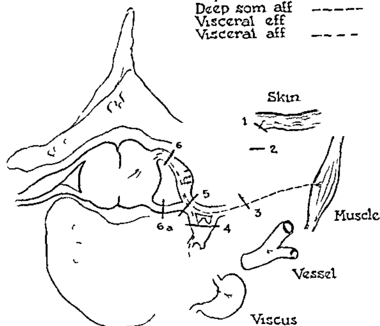


FIG 1 —Peripheral pathways for pain and possible sites where they may be blocked *1* infiltration block intradermally and subcutaneously *2* field block *3* somatic nerve block *4* autonomic ganglion block *5* somatic paravertebral or epidural block *6* and *6a* intrathecal or spinal block (Figs 1 5 6 7 and 10 from S Clin North America 35 9 1955 courtesy of W B Saunders Company)

posite side may prove very helpful One of the most useful tools in the performance of therapeutic blocks is the x ray By means of it, the localization and placement of a needle point is greatly simplified And the use of a contrast solution like Diodrast (iodopyracet) after the block needle has been placed is valuable in

predicting the spread of any solution that may be instilled through the needle It is judicious to employ x ray localization and evaluation of spread with Diodrast (after a test for sensitivity) before injecting a neurolytic solution like absolute alcohol or 6–10 per cent phenol

5 Aside from the requisite knowledge of the pharmacology of the different agents used in the performance of blocks patience is both a virtue and a valuable asset which sustains the physician in his moments of frustration in this type of work With patience, rapport may be established with the patient, and confidence gained Such a relationship seems to augment the efficacy of a block

DIFFERENT TYPES OF BLOCKS AND TECHNICS

Nerve blocks are limited to the accessible peripheral nerve trunks extending all the way from the proximal radicular portion where they lie freely in the spinal canal in the peridural space, in the paravertebral area and along their course into their terminal branches (Fig 1)

INTRATHECAL NERVE BLOCK

The instillation of a local anesthetic into the subarachnoid space has long been employed to produce anesthesia for surgical procedures The effects of a small amount of local anesthetic introduced into the intrathecal space are quite profound In view of the marked analgesia which develops one might state that this type of regional block is almost ideal as a

method for the interruption of pain pathways Yet there are so many factors involved in the controllability of any solution instilled into the spinal canal that the value of this procedure in the management of pain in malignancy may be questioned To cite an instance a negligible amount of local anesthetic introduced into the lumbar area will, in addition to causing marked anesthesia affect the motor nerves so extensively as to cause profound paralysis In the management of pain paralysis may be undesirable unless it is already present. Of course it is possible to employ a relatively weak anesthetic solution so as to spare the more highly *myelinated motor roots It is also possible to control* the degree of spread of solution to some extent, by instilling the drug through a catheter as in continuous spinal anesthesia The limitation of this method lies in the length of time the catheter may be left in the subarachnoid space without leading to serious complications such as meningitis or arachnoiditis or, for single dose spinals in the number of times the procedure may be repeated without developing the same complications

Intrathecal Alcohol

By a propitious combination of certain anatomical and physical factors it has been found possible to instill minute amounts of absolute alcohol into the spinal canal and selectively destroy sensory roots without affecting the motor roots to any great degree if at all. The different factors that make this procedure practicable are

1 All the sensory roots are in the dorsal position
2 All pain fibers have their primary neuron in the dorsal root ganglion, and so they must essentially run through the dorsal root in their course to the posterior horn
3 Absolute alcohol is hypobaric, that is it has a specific gravity of 0 810 as compared to spinal fluid which has an average specific gravity of 1 007 Alcohol will therefore float in spinal fluid
4 The spinal cord is more or less fixed in position and is anchored to the dura anteriorly by the dentate ligaments

Considering all these facts it is obvious that it is possible to introduce small amounts of absolute alcohol very carefully into the spinal canal without involving the spinal cord itself the motor roots and the sympathetic fibers that run in them by way of the white rami communicantes Going one step farther, the spinal canal may be placed in such a position that only the posterior roots of one side and a small segment thereof may be affected (Fig 2)

The method of performing the intrathecal alcohol block is quite simple and is nothing more than a modification of the usual technic of introducing a spinal needle into the intrathecal space The position of the patient is very important The spinal segment and the posterior roots involved in the pain pattern are determined first The patient is placed on an operating table which can be made to assume various positions and he lies prone with the segment to be blocked in the highest position In other words if the spinal

segment is between T5 and T8 on the right side this area is elevated by having the patient lie prone with this thoracic segment over the "break" or the kidney rest of the table Sandbags or pillows may be employed to accentuate the scoliosis so that the head the



Fig 2 —Position of patient for intrathecal alcohol injection Upper sketch shows distribution of alcohol affecting posterior roots only

neck and the rest of the body are below the elevated segment The table is then tilted so that the side of the body to be blocked (the right side) is higher than the other side without the body actually assuming a completely lateral position Bonica figures this angle to be about 45 degrees The patient is fixed or "strapped down" in this position to minimize inadvert

ent movements which may cause the alcohol to spread to contiguous areas Since the patient will have to stay in this position for at least 1–2 hours putting him to sleep may help relieve the discomfort of the situation

A short beveled 22 gauge spinal needle is employed to perform the puncture Once the resistance of the ligamentum flavum is felt the stylet is removed and a drop of local anesthetic or normal saline is placed on the hub The needle is gently pushed in until the epidural space is reached this is indicated by the sucking in of the drop in the hub of the needle An empty 2 cc syringe is now placed on the hub of the spinal needle and gentle traction maintained on the plunger as the needle is pushed forward slowly By this method as soon as the dura is penetrated, spinal fluid is aspirated into the syringe and the needle is stopped at this point It is necessary to make certain that the bevel of the needle is just within the dura This may be accomplished by exerting gentle traction on the plunger of the syringe and pulling back the needle once more until no spinal fluid returns which signifies that the needle point is just out of the dura and then pushing the needle in again slowly until aspiration of spinal fluid just becomes possible Then the alcohol is instilled At the most 0 2–0 75 cc of absolute alcohol may be used The smaller the volume the less the possibility of causing complications An average of 0 5 cc is employed A *dry* 2 cc syringe with markings showing 0 1 cc per line may be employed Or if greater precision is desired a tuberculin syringe may be used instead (Emphasis is made on the use

of a dry syringe since it is a little difficult to draw alcohol with a wet syringe) The alcohol is injected very slowly at a rate of not more than 0 1 cc per minute The patient must be warned beforehand that, as the alcohol is instilled a sensation of warmth and severe pain will be experienced over the dermatomes to be blocked He is cautioned not to move at all during this period and is informed that this sensation is momentary

Following the injection of the alcohol the patient is left in this same position for at least 1–2 hours after which he may be turned into the supine position It is preferable to have the patient lying in bed for the next 12–24 hours The effects are immediately apparent if successful although a few days later the patient may experience a sensation of hyperalgesia or hyperesthesia this usually disappears A disconcerting burning" sensation may develop which may be relieved by paravertebral sympathetic block

Complications may arise occasionally depending on the site of the injection In the lumbar area for example it is not uncommon to find weakness of an extremity or paralysis of the sphincter of the bladder and rectum In the neck and upper thoracic areas weakness of an upper extremity may develop Such weakness or sphincter paralysis disappears after a period of 3–6 weeks

The intrathecal alcohol block is probably most useful in patients who are not physically capable of withstanding a neurosurgical procedure for the interruption of pain pathways The block may be repeated

without necessarily causing any serious complications In fact, if an extensive area is involved in the pain pattern it may be wise to block off small segments at a time If both sides are afflicted one side may be blocked first and the other side treated after an interval of a week. A trial block with a local anesthetic like hypobaric pontocaine (tetracaine) might be utilized before alcohol is used, in order to acquaint the patient with the analgesia that develops Hypobaric pontocaine is a solution containing 1 mg per cc of distilled water and having a specific gravity of 1 003

A 27 year old woman was referred to the anesthesia department complaining of pain radiating to both lower extremities but more severe on the left side She had had an abdominoperineal resection for carcinoma of the rectum Despite the extensive resection metastases had apparently extended to the sacral area probably involving parts of the lumbosacral plexus of nerves She had had a colostomy and an indwelling urethral catheter had been introduced In view of her poor physical condition and what was felt to be a terminal state of the disease an intrathecal alcohol block to the left lower extremity was first decided on A trial injection of hypobaric pontocaine was made to familiarize the patient with the effects of the block She was placed in the prone position with the left lumbar area uppermost for the alcohol injection Absolute alcohol 0 5 cc was instilled, the introduction of the entire amount taking about 6 minutes Relief of pain was immediate and complete The following complications were noted weakness of the left lower extremity and a burning sensation radiating down the left leg The burning pain was suggestive of a sympathetic type of pain A week later a paravertebral block of 1 2 3 sympathic ganglia was performed using 6 per cent phenol The burning pain was completely

relieved Intrathecal alcohol block to the right side was contemplated but it was decided to wait for the disappearance of paresis of the left leg However the patient developed metastases in the lungs and died before the right side could be blocked

The subarachnoid injection of alcohol is considered a major procedure and should be done in the operating room In spite of the seeming simplicity of the method serious complications may develop from the bungling efforts of the uninitiated No one should attempt this procedure without being thoroughly familiar with the technical and physiologic details associated with the administration of a spinal block

Epidural Block

The epidural space is a potential cavity limited cephalically by that portion of the base of the skull to which the dura is anchored, laterally by the intervertebral foramina anteriorly by the body of the vertebrae and caudally by the sacrum and its openings Any solution instilled into this potential cavity will thus tend to follow the path of least resistance and spread in a cephalad and a caudad direction and laterally following the intercostal nerves It is difficult to control the spread of any solution introduced into this space, and the introduction of necrotizing solutions may therefore be dangerous, inasmuch as large volumes are necessary to be effective and small volumes may be futile

The epidural block is of limited value in the man

agement of pain in malignancy In terminal stages of the disease it is possible to introduce a catheter into the epidural area and inject local anesthetic solutions at intervals of four to eight hours and thereby relieve pain Granulation tissue develops around the tip of the catheter and plugs it within a period of 48–72 hours so another catheter may have to be inserted Considerable relief of pain may be afforded the patient in this manner, but prolonged use of the epidural catheter is impractical since the continuous presence of this foreign body encourages the development of infection along the path of the catheter

Peripheral Nerve Blocks

As previously stated nerves may be attacked along their course from their point of exit to the periphery Anatomically and physiologically most peripheral nerves are mixed nerves (motor and sensory) and blocking them interferes with their motor function In certain areas of the body, some major nerves are predominantly sensory, like the trigeminus (5th cranial nerve) If mixed and blocked the motor activity that normally results from the influence of the motor fibers may be carried on by neighboring structures (for example intercostal nerves) Another anatomic fact of importance is that the bony landmarks are valuable in locating these nerves X ray examination may prove very useful in determining whether the needle point is in close proximity to the nerve in relation to the bony landmarks

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reflex vasoconstriction furthering the hypoxia Relief may be obtained by interrupting vasoconstrictor fibers in the sympathetic system Lastly sympathetic plexuses and ganglia are very accessible and quite vulnerable to mild necrotizing agents considering their poor myelin covering

AGENTS USED FOR BLOCKS

There are two main groups of agents employed in performing blocks for pain of malignancy (1) local anesthetic agents and (2) nerve necrotizing agents

Local Anesthetic Agents

The local anesthetic drugs available are so numerous that one is frequently faced with the problem of selecting one agent from among several that may be equally good Final choice however, is frequently dictated by certain criteria referable to the drug such as (*a*) rapid onset of action (*b*) low toxicity (*c*) long duration of action (*d*) nonirritation of tissues (*e*) profound analgesia and (*f*) selectivity of effect Other factors, referable to the physician employing the drug must also be considered—for example (1) familiarity with the drug (2) availability of drug (3) cost of drug (must be relatively cheap) and (4) a prejudicial preference for the agent Not all the criteria referable to the drug can be satisfied by any one agent, but a combination of two or three drugs may satisfy all or most of them For instance mixing 0 25 per

The cranial nerves may be blocked at their point of exit from the foramina at the base of the skull The intercostal nerves may be blocked paravertebrally as they emerge from the intervertebral foramina at the angle of the ribs posteriorly between the line joining the midline vertebral spines and the medial border of the scapula or at the posterior axillary line The cervical nerves are vulnerable as they wind anteriorly over the transverse processes Blocking the spinal nerves in the paravertebral area, however may involve certain dangers and complications It is not too difficult to introduce the anesthetic agent into the subarachnoid space by inserting the tip of the needle into a dural sleeve or as Moore has shown injecting directly into the nerve through the epineurium enabling the drug to find a passage into the intrathecal canal But a necrotizing agent inadvertently introduced into the spinal canal may cause serious complications such as arachnoiditis or transverse myelitis with a concomitant paralysis

Sympathetic Nerve Blocks

The sympathetic nerve block may prove useful in the control of pain referable to a viscus As mentioned previously pain fibers from most visceral organs travel by way of the sympathetic plexuses and ganglia but do not necessarily form synaptic connections Accordingly, visceral pain fibers may readily be interrupted by a sympathetic block The other mechanism of pain in a viscus is distention which causes hypoxia and

NERVE NECROTIZING AGENTS

These agents exert their effect by destroying the nerve fiber or the cell It has been established that necrosis of the nerve fiber extends all the way back to the first node of Ranvier The nerve cell of a somatic nerve may remain intact, thus implying that regeneration of the nerve fiber is not an impossibility The relief afforded by these agents is therefore only relatively permanent Three agents have been outstanding ethyl alcohol, phenol and ammonium sulfate Ethyl alcohol has been employed in concentrations varying from 50 per cent to absolute The best concentration to use is the absolute alcohol because lower concentrations tend to give unpredictable results Although the incidence of neuritis is high after a block with ethyl alcohol the results when successful are so gratifying that the risk is considered worth while Ethyl alcohol has a very limited degree of spread in the tissues Experimentally 5 cc of alcohol injected into muscular tissue will cause a necrosis 1 cm in diameter If injected into a fascial plane of course the spread may be greater and may follow the course of a nerve Partial or incomplete relief of pain after an alcohol block may be ascribed to improper placement of the needle use of an insufficient amount of alcohol or dilution of the alcohol by the previously instilled local anesthetic agent Phenol (6 per cent) acts very well on sympathetic nerves and it may be employed in greater volumes than alcohol Higher concentrations of phenol up to 10 per cent may be employed if the solution is

cent pontocaine with 2 per cent procaine will give an agent that is rapid in onset (due to procaine) and has low toxicity, profound analgesia and relatively long duration of action. It may have a poor selectivity of action in that it indiscriminately affects motor, sensory and sympathetic nerves, but it satisfies most of the factors referable to the physician employing the drug. Prejudicial preference for a local anesthetic agent may exert an unduly large influence in the selection of the agent to be employed.

The value of local anesthetic agents in malignancy lies in their usability for differential diagnosis. Depending on the concentration of the drug or the placement of the needle, it may be possible to establish whether somatic sensory pathways or sympathetic pathways or both are involved, and by means of local anesthetics it may be possible to determine which or how many of the sensory nerves supplying an affected area are involved. Repeated blocks with local anesthetic agents at regular intervals may diminish the pain considerably. This may also be accomplished by introducing a plastic catheter in the immediate vicinity of the nervous structure to be blocked. During the performance of an alcohol block the previous instillation of a local anesthetic agent mitigates the intense pain associated with the introduction of alcohol into the tissues, as well as the pain from the insertion of the block needle itself. A preliminary local anesthetic block of the nerves to a painful area enables the patient to evaluate the loss of sensation that may develop with a more permanent type of block.

(5th cranial) nerve Interruption of any of the three divisions of this nerve—mandibular, maxillary and ophthalmic—as they emerge from their respective foramina at the base of the skull will control pain from these regions If all three divisions are involved,a gasserian ganglion block may be the method of choice Injection into the gasserian ganglion implies interruption of all three divisions of the 5th nerve, so that the ophthalmic division which supplies all sensory elements of the area around the eye and the eye itself is affected A serious complication of this procedure is keratitis and even ulceration of the cornea Where life expectancy is not too long such a complication may not be too great a price to pay for the ensuing relief of pain In occasional instances when the eye is involved, a block of the ophthalmic division or the gasserian ganglion may be done with relative impunity

A 67 year old man with an invasive slow growing epidermoid carcinoma of the face which had completely involved the left eye and its socket was brought to the operating room for excision of the metastatic growth invading the eye socket The chief complaint was severe pain in this area During the procedure the opinion of the anesthesiologist was solicited for whatever extra procedure might be performed to alleviate the pain Extensive excavation of the left eye socket had been performed and closer scrutiny disclosed the ready accessibility of the gasserian ganglion Injection of absolute alcohol into the area of the gasserian ganglion was advised and subsequently performed Relief of pain was complete

Tumors may also arise from the paranasal sinuses Again pain develops as a consequence of compression

warmed in order to increase the solubility of the phenol As much as 20–25 cc of 6 per cent phenol has been instilled in the splanchnic area for a celiac plexus block Even though sympathetic nerves are very vulnerable to necrotizing agents they regrow so fast that phenol instillation may have to be repeated more *frequently than alcohol instillation Ammonium sulfate* has been used most frequently in concentrations of 0 75–2 0 per cent This agent was thought to have a selective action on somatic sensory nerves but it has not come up to expectations A concentration of 6 per cent is believed to be more effective

Whenever these necrotizing agents are employed it is wise to use x rays to help localize the site of the needle point and if possible to instill a contrast solu tion like Diodrast prior to instillation of alcohol or phenol in order to be able to predict the spread of these agents

BLOCKS FOR DIFFERENT REGIONS

HEAD AND NECK

Malignant growths frequently involve the different structures of the face the mouth and its contained organs, the neck and the throat Pain results from pressure on sensory nerve structures or involvement of the nerve structures themselves In the facial area tumors may develop from the skin especially around the mouth and nose or from the sinuses in the para nasal area Pain impulses from this area are mediated through the three main divisions of the trigeminal

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or of actual involvement of branches of the trigeminal nerve Tumors in this area frequently affect the maxillary and the mandibular divisions Blocks of these branches are easily accomplished where the branches emerge from their respective foramina In blocking these divisions paresthesias may be used to ascertain the position of the needle point Instillation of 1-2 cc of a local anesthetic agent followed by development of anesthesia or analgesia over the facial segments supplied by these nerves offers some degree of re assurance of the proper position of the needle point Three cc of absolute alcohol may then be instilled to produce a permanent block In addition to utilizing paresthesias *x ray study is valuable in executing this* type of block With the head in the proper position a good x ray picture diminishes the element of chance in placing the needle It is quite simple to demonstrate the needle point close to or at the foramen rotundum for the maxillary nerve and the foramen ovale for the mandibular nerve (Fig 3)

Malignant tumors may also develop in the tongue the buccal mucosa and the salivary glands Tumors arising in the tongue occasionally pose a complex problem in pain control because the tongue is in nervated by several nerves The anterior two thirds of the tongue is innervated by the mandibular division of the 5th cranial nerve by way of its terminal branches—the lingual nerve The posterior third is supplied by the glossopharyngeal nerve Nerve twigs also come from the cervical plexus Thus should the pain arise from a site common to both the trigeminal

and the glossopharyngeal nerves blocking both may be necessary to relieve the pain If some pain persists after blocking both the 5th and the 9th cranial nerves it may be necessary to interrupt spinal nerves C2 and C3 Tumors of the mandible may of course give rise



FIG 3 —X ray of base of skull showing needle (*A*) with point close to foramen rotundum (*B*) for maxillary nerve block

to pain referable to the mandibular division of the trigeminal nerve and to C2 C3 and possibly C4

In discussing pain as a complication of malignant tumors of the face mouth paranasal sinuses and mandible one frequently loses sight of the fact that after the malignant growth has been radically excised and possibly eliminated grossly pain may persist post

operatively The misery provoked by this persistent pain may make the patient almost as unhappy as having the original tumor Pain may also develop after irradiation of the tumor area or after radon seed implantation

A 70 year old man had a tumor on the dorsum of the right half of the tongue Apparently the tumor was of a low grade type of malignancy with no metastases to lymph nodes or contiguous structures The tumor was excised and recovery from the operation was uneventful However postoperative pain developed The patient was referred to the anesthesia service and the following procedures performed A lingual nerve block with tetracaine was performed to find out how much relief could be obtained Relief of pain was immediate and considerable and lasted for about 48 hours As a result an alcohol block was performed employing 2 cc of absolute alcohol Relief was good but a burning type of pain developed on the dorsum of the tongue Since it seemed that the nerve had been only partially destroyed by the alcohol instillation another injection of absolute alcohol was made in the area of the lingual nerve two weeks after the first injection but the burning pain persisted The relief of the original knife like pain at the site of the incision lasted for a period of two months after which the pain returned An extraoral mandibular nerve block was executed with 3 cc of absolute alcohol abolishing the pain at the site of the incision but leaving a sorenes e posterior third of the tongue extending dow ngeal area This distribution butable al nerve

year from an extensive tumor base of the tongue radiation therapy ain developed

over the irradiated area It was burning in character and thought to be mediated through sympathetic pathways A stellate ganglion block was performed and complete relief of pain was obtained In view of this 8 cc of 6 per cent phenol was instilled into the region of the stellate ganglion under x ray control Pain relief was not as complete as with the local anesthetic but at least 75 per cent relief was experienced

In the neck and lower jaw pain developing from malignant tumors of the mandible the submaxillary glands the thyroid and the larynx may give rise to varying degrees of pain For pain arising from the mandibular area a mandibular nerve block reinforced by injection of the deep cervical plexus (C2 3 4) will provide pain relief in most instances For pain in the area of the neck a block of the deep cervical plexus will be satisfactory in most instances except for the larynx and the esophagus These structures receive their sensory innervation from the vagus through the superior and inferior laryngeal nerves respectively Any standard text on regional blocks will show that it is relatively easy to block the superior laryngeal nerve

In the region of the neck extensive necrosis or radical surgery frequently defiles the area so extensively that landmarks necessary for the proper execution of the above-mentioned blocks may be obliterated The instillation of absolute alcohol intrathecally may be valuable—in fact this may be the only means available for providing relief from pain in the terminal stage aside of course from massive doses of analgetics which may not be effective at all

UPPER EXTREMITY

The brachial plexus which derives its origin from the anterior primary divisions of the spinal nerves C5, 6 7 8 and T1 supplies the chief innervation to the upper extremity Sympathetic innervation (post ganglionic fibers) comes from the stellate ganglion the middle cervical ganglion and paravertebral gang lia T2 3 and 4. Malignant tumors in the neck may involve the divisions and trunks of the brachial plexus and provoke severe pain referable to the upper ex tremity Tumors of the dome of the lung frequently involve the brachial plexus causing severe pain trophic changes in the arm and paresis or paralysis Aside from injecting absolute alcohol into the intra thecal space there is no satisfactory way of relieving pain in these patients Injection into the brachial plexus necessarily produces complete paralysis of the extremity even if analgesia is provided Some patients with pain arising from involvement of the brachial plexus feel that they should try to preserve whatever function remains in the extremity It is rather pathetic and difficult to convey to them that the situation is progressive and not static and that complete paralysis of the extremity will develop eventually A stellate ganglion block or block of T2 3 and 4 ganglia may diminish the pain to some extent This may be ex *plained by improvement of the blood supply to the* extremity through dilation of blood vessels thus relieving somewhat the hypoxic condition

THORAX

Tumors arising in the tracheobronchial tree and affecting the bronchus, esophagus other structures in the mediastinum or thoracic vertebrae often cause pain in the thoracic area Relief of pain arising from involvement of the viscera in the thorax is rather unpredictable and complete relief is seldom obtained This may probably be explained by the fact that thoracic visceral innervation is so inextricably complex that huge areas have to be blocked frequently to obtain any semblance of relief All too often, one is tempted to ascribe all sensory thoracic visceral innervation to the sympathetic division of the autonomic nervous system although it is known that quite a number of the sensory fibers travel with the vagus The relative inaccessibility of the plexuses in the thoracic cavity increases the difficulty of relieving pain arising from thoracic viscera One mitigating factor is the fact that the cervical sympathetic ganglia contribute many fibers to the formation of the bronchial and cardiac plexuses especially the middle cervical and the stellate ganglia These ganglia are situated where they are readily accessible to the block needle The other factor is that the vagus nerve as it emerges at the base of the skull is quite vulnerable As far as intrathoracic viscera are concerned pain arising from these structures may be relieved by blocking the sympathetic ganglia the vagus nerves or both The upper parts of the esophagus and the tracheo

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pect of the trachea and the vertebral body—that is, between the trachea and the artery Bony contact is established with the transverse process of the 7th cervical vertebra in most instances After making sure by aspiration that a vessel has not been entered the

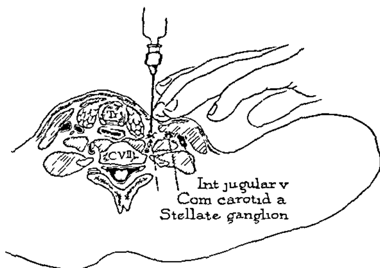


Fig 4 —Anterior approach for performance of stellate ganglion block

local anesthetic solution is injected Five to 10 cc of local anesthetic solution is sufficient to produce a block of the ganglion by diffusion By this approach the needle point is usually introduced into the same fascial plane as the stellate ganglion The appearance of Horner s syndrome—miosis ptosis conjunctival in jection and relative enophthalmos—assures the proper placement of the needle point There is also dryness

bronchial tree receive fibers from the stellate and middle cervical ganglia and the upper three or four thoracic ganglia

STELLATE GANGLION BLOCK —The stellate ganglion may be blocked by any of *four* approaches It may be approached from the *posterior* aspect this is very similar to performing a paravertebral block This method is not very popular, and the danger of penetrating a projecting dural sleeve along the cervical spinal nerve is ever present The ganglion may be approached from the *lateral* aspect of the neck The needle point is directed to contact the body of the 7th cervical vertebra or the 1st thoracic vertebra The lateral approach always seems to be quite formidable in view of the number of structures that intervene as the block needle traverses the region between the skin on the lateral aspect of the neck and the body of the 7th cervical vertebra, and this approach has lost its popularity Volpitto and Risteen modified this procedure by advocating an *anterolateral* approach which is quite similar to the lateral approach except that it utilizes more landmarks The most popular method of performing the stellate ganglion block is by way of the *anterior approach*

In the anterior approach (Fig 4) on a point located 1–1½ in above the space of Burns, the index finger is insinuated between the trachea and the sternocleido mastoid muscle on the side to be blocked at the same time feeling for the carotid artery The trachea is pushed medially and the carotid artery more or less laterally The needle is inserted along the lateral as

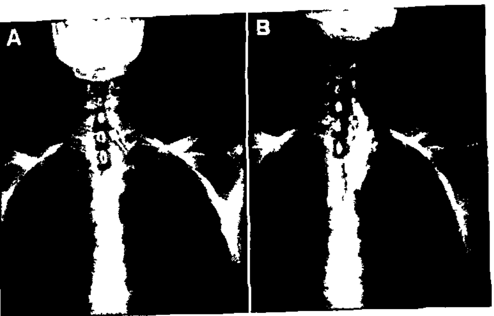


FIG 5—*A* stellate ganglion block with needle point on transverse process of T2 *B* same block after injection of Diodrast showing cephalad spread sufficient to block stellate The needle placement in this block was unnecessarily low However the objective was to try to catch the sympathetic components of T3 and T4 with one block in this patient who had a causalgia of left arm Six per cent phenol gave complete relief

of the face on the side blocked and stuffiness of the nose It is interesting to note a patient perspiring only on the contralateral side after a stellate ganglion block

If a stellate ganglion block relieves pain in the head and neck area the upper extremity or the upper thoracic area, a necrotizing agent should be instilled to provide for a longer duration of relief Absolute alcohol may be employed However experience has *shown that 6 per cent phenol provides a very satisfactory* agent for necrotizing the stellate or any sympathetic ganglion since it does not provoke as much irritation as absolute alcohol Thus relatively larger amounts of phenol solution may be instilled in the region of the stellate ganglion providing for a greater margin of success As previously mentioned x rays should be utilized in localizing the placement of the needle point and predicting the spread of solution by instilling Diodrast into the area to be blocked (Figs 5 and 6) As much as 10 cc of 6 per cent phenol has been instilled into the area of the stellate ganglion without causing any apparent damage to surrounding structures The solution may spread from the immediate vicinity of the stellate ganglion along fascial planes to affect the middle cervical ganglion and caudally as low down as sympathetic ganglia T2 and T3

As in any other block, complications develop occasionally Rarely a pneumothorax occurs or an intrathecal injection is made by the anterior approach to the stellate ganglion The carotid may be punctured though this is not any more serious than performing a carotid puncture deliberately for arteriography The

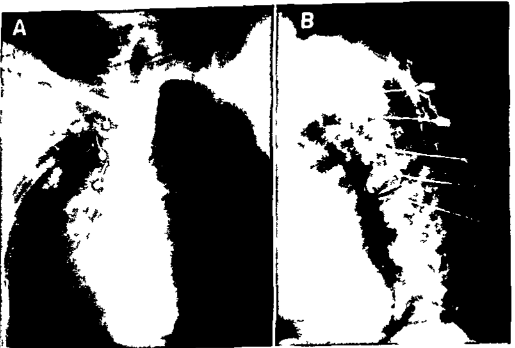


FIG 7—*A* anteroposterior view of upper thoracic paravertebral blocks with needles in position *B* oblique lateral view of same patient after injection of Diodrast solution

recurrent laryngeal nerve may be involved causing some amount of hoarseness On the right side the esophagus may be affected and give rise to some dysphagia Whenever phenol or alcohol is used to



Fig 6 —Stellate ganglion block with needle on C6 Lateral approach was used Diodrast injection showed a cephalad spread to the middle cervical ganglion and a caudal spread down to T2

cause necrosis of the stellate ganglion the subsequent ptosis and miosis may persist for some time Chemical lysis of a nerve or ganglion or plexus is not as permanent as one might be led to believe for nerves and ganglia regrow rapidly after chemical interruption

A good indication of regrowth is recurrence of the original pain, and one should not hesitate to repeat the block with a neurolyzing agent whenever the pain occurs The effects of a chemical sympathectomy may last from one week to as long as six months If a surgical sympathectomy is attempted after a chemical sympathectomy the surgeon often has much difficulty in locating the sympathetic ganglia

PARAVERTEBRAL SYMPATHETIC BLOCKS —To obtain relief of pain lower down in the thorax especially of the viscera paravertebral sympathetic blocks may have to be performed The technic is relatively simple and was originally devised by Kappis The approach is posterior and involves the introduction of the block needle on a point lateral to the midline by 1½–2 in opposite the intervertebral foramina Actually some authorities prefer to raise the wheals opposite the vertebral spines 1–2 cm from the midline establish contact with the lamina and slide off the lamina into the intervertebral foramen This approach has been found very successful in most instances

A local anesthetic should always be employed first in blocks of this kind whenever a more permanent type of procedure is contemplated The kind of local anesthetic to be used is beside the point What is important is that the instillation of a local anesthetic gives an idea of how much relief may be obtained with the contemplated block and at the same time familiarizes the patient with the effects of a block Occasionally repeated blocks with a local anesthetic may afford a considerable amount of relief of the pain

block the nerve and viscera A somatic nerve block in the thoracic area may have to be performed if a tumor has invaded the pleura or thoracic wall and is causing severe pain In view of the extensive overlapping of spinal nerve distribution in the thoracic area, several of the nerves may have to be blocked If for example the pain is confined definitely to T7, blocking T6 and T8 will give a greater degree of pain relief than just blocking T7 Where tumor tissue has invaded the spine involving the nerves as they come out of the dura a paravertebral block is definitely out of the question The only procedure that may afford some relief aside from neurosurgery is probably intrathecal injection of absolute alcohol

An aspect of thoracic pain in malignancy that should not be lost sight of is post thoracotomy pain This condition is frequent and the patient may suffer as much from it as from the original malignant condition for which he was operated on A paravertebral block of the nerves supplying the area of the incision may eliminate or mitigate the pain

INTERCOSTAL NERVE BLOCK —The value of this type of block is limited If the pain is confined to the anterior aspect of the chest and is superficial or can be demonstrated to affect the thoracic wall predominantly this block may be useful The intercostal nerve block is easily performed It may be done posteriorly at the angle of the ribs at the posterior axillary line or at the midaxillary line Occasionally, where the pain is confined to the sternal area the block may be done at the anterior axillary line

picture In most instances, the patient complains of being numb and sore over the same area Numerous remedies for the neuritis have been suggested, such as reblocking the affected nerve, although the original block was intended only for the sympathetic ganglion Some authors have suggested instilling procaine after the alcohol block before pulling out the needle, others have given procaine or pontocaine by intravenous drip to relieve the pain (1 Gm procaine in a 0 2 per cent solution)

It is possible inadvertently to enter a prolonged dural cuff causing instillation of a necrotizing agent into the spinal canal A Brown Sequard type of paralysis has been reported Therefore it is wise to have the patient lie on his side after instillation of a necrotizing agent in case some of it may have been introduced into the intrathecal space Because alcohol is hypobaric and will float in spinal fluid, it affects only the radicles in the uppermost portion should it enter the subarachnoid space Similarly most local anesthetics employed for blocks are usually hypobaric In performing paravertebral blocks, therefore the area to be blocked should be situated superiorly so that any anesthetic agent injected into the subarachnoid space accidentally during a paravertebral block will be confined to the upper portion of the spinal canal and thus affect only the rootlets in that area

Anatomically, the somatic nerve in the thoracic area is located very close to the ganglion as it lies in the intervertebral foramen. It is obvious as was pointed out previously that a block of the ganglion may also

the breast A type of pain frequently seen in the thoracic area is that which follows radical mastectomy and is confined to the axillary region in most instances Pain may be relieved by a paravertebral block or an intercostal nerve block of spinal nerve T2 at the posterior angle

EPIDURAL NERVE BLOCK —Occasionally severe pain referable to the thoracic wall may be so extensive as to render paravertebral and intercostal blocks impractical An *indwelling catheter* introduced into the epidural space may help considerably in controlling such a wide area of pain as this In the terminal patient suffering intensely from severe pain over a wide area the indwelling epidural catheter may be very valuable in relieving pain Local anesthetic solutions may thus be injected at regular intervals The volume of anesthetic agent employed depends on the size of the area involved and the resistance that the patient may develop to the drug

ABDOMEN

Pain fibers from the abdominal viscera travel by way of the sympathetic nervous system although the primary neuron lies in the posterior root ganglion (see Fig 1) Therefore visceral pain from the abdomen may be relieved by interrupting sympathetic pathways by means of paravertebral blocks in the thoracic area or by a splanchnic block

SPLANCHNIC BLOCK.—This term is probably a misnomer since there are three splanchnic nerves—a

The intercostal nerve is located all the way along its course from the intervertebral foramen to the sternal edge anteriorly under the inferior border of the rib The bony rib is therefore the chief landmark in performing this block The outer surface of the rib is contacted with the point of the needle preferably at the posterior angle The needle is then made to slide over the lower border of the rib and the solution instilled In obese individuals the posterior angle of the rib may be hard to palpate making the block a little more difficult to perform Under such conditions it is preferable to make the block at the posterior axillary line Three to 5 cc of solution is enough to anesthetize the nerve The incidence of neuritis after the instillation of a necrotizing agent into the region of the intercostal nerve is quite high Aside from this complication the pleural cavity may be entered and the lung punctured causing a pneumothorax However such a complication is not too serious provided the patient is kept quiet in bed The air in the thoracic cavity is eventually absorbed and the pleural tear sealed off Occasionally a tension pneumothorax may develop in which case the air may have to be evacuated An 18 gauge needle attached to a three way stopcock and a 20 cc syringe are sufficient to accomplish this procedure

Malignant tumors of the thoracic cage provoking pain are probably not too frequent. They may be invading growths from tumors of intrathoracic viscera or tumors arising from the bony cage or occasionally invasion of the thoracic wall by malignant tumors of

If the back is broad or the 12th rib is not palpable the spine of the 1st lumbar vertebra is located and a point 2½–3 in lateral to it is used as the point of insertion The block is best performed with the patient

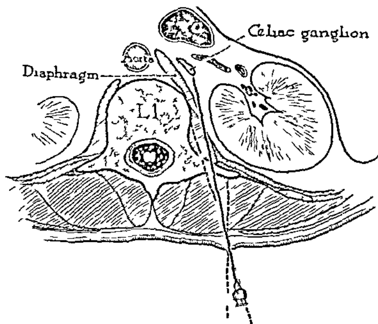


Fig 8 —Cross section at L1 showing needle point in vicinity of celiac ganglion

lying in the lateral or the prone position As soon as the point of insertion has been decided on a skin wheal is raised at this site and the block needle introduced at an angle of about 30 degrees to the median sagittal plane at the same time aiming for the body of the 1st lumbar vertebra Frequently the

greater, a lesser and a least splanchnic nerve What is significant is that all three traverse the largest sympathetic plexus in the body, known as the celiac or solar plexus Aside from the splanchnic nerves the vagi especially the right vagus send branches to it The celiac plexus is located at the upper border of the first lumbar vertebra and is intimately related with the celiac and superior mesenteric arteries Actually *therefore a splanchnic block, as performed, is more* a celiac plexus block than anything else A good celiac plexus block will interrupt most intra abdominal visceral pain pathways (Fig 8)

There are two outstanding approaches to the splanchnic plexus—anterior and posterior The *anterior approach* necessitates entry into the abdominal cavity and is best performed by the surgeon during the course of the operative procedure It was first advocated by Braun and involves injecting a local anesthetic into the region of the 1st lumbar vertebra between the inferior vena cava and the abdominal aorta

The *posterior approach* was developed by Kappis and obviously entry into the abdominal cavity is not a requisite The landmarks are the 12th rib the spine of the 1st lumbar vertebra and the transverse process of the 1st lumbar vertebra Depending on the breadth of the patient s back, any one of two points may be utilized as the site of insertion of the long (6 in) block needle that is employed If the patient s back is rather narrow and the 12th rib easily palpable this rib is a good landmark, and its inferior border may be used as the point for inserting the needle

provokes is much less than with absolute alcohol As much as 30 cc of 6 per cent phenol has been employed at one time For psychologic reasons it may be best to perform the block on the side presenting

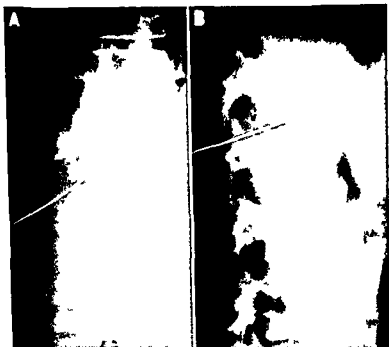


Fig 9—A anteroposterior view showing needle point at lower border of T12 and Diodrast spread from T11 to L2 B lateral view of same injection

the most pain If pain still persists on the other side a splanchnic or celiac plexus block may be done after an interval of one week

The scope of the celiac plexus block is extensive It may relieve pain caused by malignant tumors of

transverse process of the 1st lumbar vertebra may be encountered in transit If so the needle is redirected either cephalad or caudad to by pass the process As soon as contact with the body of the 1st lumbar vertebra is established the needle is withdrawn and redirected at a more acute angle in relation to the median vertical plane, until the vertebral body is again contacted This procedure is repeated until the needle point is felt to slide off the bone As soon as bony contact is lost the point of the needle is most probably in the same fascial plane as the celiac plexus

The solution may then be instilled into the area If a permanent type of block is contemplated, x rays should be used Films in both the anteroposterior and lateral positions should be taken after placement of the needle (Fig 9) If the needle point is in good position, Diodrast should be instilled to predict the spread of the necrotizing agent Diodrast may be mixed in equal amounts with a local anesthetic agent and used as such This will diminish the concentration of Diodrast and may lessen the chances of a reaction to Diodrast The amount of Diodrast solution employed should approximate the amount of necrotizing agent to be injected into the area, the average amount employed is 10 cc If the spread of the Diodrast solution is satisfactory, the neurolytic agent may be introduced It is advisable to wait 10–20 minutes in order to assure absorption of the Diodrast Six per cent phenol the preferred necrotizing agent works very satisfactorily on sympathetic nerves and ganglia and the amount of neuritic phenomena it

the pancreas liver stomach, duodenum small bowel mesentery and other upper abdominal structures but the relief afforded is unpredictable Depending most probably on how much of the plexus is affected by the agent, the relief may last anywhere from a week to a year

A man 65 had an inoperable carcinoma of the stomach with metastases to the liver Gastrostomy was performed The patient complained of continuous, unrelenting pain in the epigastric area A splanchnic block was performed eliminating 80-90 per cent of the pain It improved his appetite allowing him to gain 5-10 pounds The relief of pain was good until his death

A woman 45 had a pancreatic tumor which was not resectable She complained of a continuous epigastric pain confined chiefly to the right side A splanchnic block was performed under x ray visualization using 12 cc of 6 per cent phenol Relief of pain lasted for one week The impression was gained that an insufficient amount of phenol was employed

Despite the seeming simplicity of the celiac plexus block, complications may develop A too cephalad placement of the needle point may find it within the thoracic cavity occasionally causing pneumothorax and it is possible to puncture the inferior vena cava or the aorta Such complications as these however are not too serious In transit to the body of the vertebra the needle may impale the kidney or the pelvis of the kidney may be penetrated The needle may find its way into the abdominal cavity which happens occasionally without necessarily causing frank



Fig 10–4 bilateral paravertebral sympathetic block with needles in position—body of L2 B after injection of Diodrast, the solution spread one segment above to L1 on the right and was more or less confined to L2 on the left

intended to interrupt nervous pathways to deep pelvic organs may seriously interfere with the motor functions of the lower extremities In a relative manner, it is anatomically fortunate that visceral pain fibers frequently travel by way of the sympathetic ganglia and plexuses Thus in the lumbar region, the sympathetic ganglia and the paravertebral plexuses are readily accessible In the deep pelvic region especially the sacral area some portions of the sympathetic nervous system become almost inaccessible, or if they are accessible they may be very intimately associated with somatic motor and sensory nerves to the lower extremity

In view of the difficulty of dissociating pain pathways from important motor nerves in the pelvic area, it may be much wiser in the fairly good surgical risk patient, to perform a neurosurgical interruption of pain pathways in the cord or higher up in the central nervous system

Occasionally pain may be confined to one side If the pain is visceral in nature—that is poorly defined or cramplike—and assuming that there is no evidence of severe bowel obstruction a sympathetic block to that side may be performed

LUMBAR PARAVERTEBRAL SYMPATHETIC BLOCK.—In performing this type of block one anatomical consideration should be kept in mind In the lumbar area the sympathetic ganglia assume a more ventral position on the vertebral body as compared with the lateral situation of the thoracic sympathetic ganglia in the intervertebral foramen Thus, the approach is

complications and the possibility of invading the intrathecal area or penetrating into a projecting dural sleeve is not too remote In addition infection may develop along the course of the needle Antibiotics should be administered routinely to patients to minimize infection

Intercostal blocks are of little value in abdominal visceral pain They may prove useful as in the chest for painful tumors of the abdominal wall or in the control of referred pain which is seldom seen in cases of pain in malignancy Again as in the thoracic cavity an indwelling catheter in the epidural space with intermittent instillation of a local anesthetic agent may prove very useful in terminal cases with severe pain

Pelvic Cavity

Pain caused by malignant tumors in the pelvic cavity not only is difficult to manage but is frequently a frustrating problem even when blocks are used The reason for this is that most malignant growths arising in the pelvic region develop from organs situated in the midline—for example the bladder the prostate the uterus and the rectosigmoid This implies a bilateral innervation Thus pain emanating from these organs is referable to both sides An associated difficulty is the close relationship of the nerve supply of the organs in the pelvic cavity with the nerve supply to both lower extremities In the lumbar area, such association is not so serious as to involve motor function extensively In the sacral area however blocks

show a rise after the block provided severe arteriosclerosis is not present in which case there may be no change in temperature and pain may develop in the extremity As with a splanchnic or celiac plexus block the complications that may develop are subarachnoid injection puncture of the vena cava or the aorta and penetration into the abdominal cavity with possible entry into a loop of bowel

In terminal conditions where neurosurgical procedures may not be feasible an intrathecal alcohol injection may be performed In these patients the disease has progressed to the point where it may be interfering with sphincter and lower extremity functions Or radical surgery may have eliminated both bladder and rectal sphincter control so that the only complication that may be considered seriously is weakness of the extremity

As an alternative a continuous peridural or caudal drip may aid temporarily in relieving the pain, but its effectiveness is limited in that either the catheter placed in the epidural space becomes plugged by granulation tissue or the patient develops resistance to the local anesthetic agent

Lower Extremities

The lumbosacral plexus which furnishes the chief nerve supply to the lower extremities lies in close proximity to the deep pelvic organs Consequently malignant tumors of these organs are highly prone to affect this plexus One of the common causes of pain

through the back and the actual procedure is similar to that of a splanchnic or celiac plexus block The chief bony landmarks are the lumbar spines the transverse processes, the 12th ribs and the iliac crests The last two are helpful in locating the position of any of the lumbar spines

Intradermal wheals are raised over the transverse processes of the lumbar vertebrae at a point 3–4 cm from the midline The needle point is made to contact the transverse process and then partly withdrawn and redirected in a cephalad and medial direction so that it slides over the transverse process The needle forms an angle of 30–45 degrees with the median sagittal plane, and it should establish contact with the body of the vertebra An attempt should then be made to coax the needle to slide off the body of the vertebra Ten cc of local anesthetic may be injected for each ganglion This block may work effectively for uterus and perhaps bladder pain For pain emanating from the areas of the rectum cervix and prostate the sacral nerves may have to be blocked, in which case the sciatic nerves may be interfered with If a lumbar sympathetic block is effective 6 per cent phenol should be employed to produce a more permanent type of block X ray study with Diodrast is valuable for establishing precision in needle placement (Fig 10) An effective lumbar sympathetic block is indicated by a sensation of warmth in the corresponding lower extremity and of course relief of pain if the pain pathway courses through the sympathetic ganglia Temperatures of designated spots on the leg will

for the incidence of post alcoholic neuritis is so high that it is doubtful whether absolute alcohol should be used at all for these peripheral nerves

A 29 year old man was referred to the anesthesiologist by the orthopedic and the neurosurgical clinics because of a persistent pain in the sole of the left foot following the excision of a painful neuroma Infiltration of trigger areas in the scar proved unsuccessful because of the denseness of the scar tissue A medial plantar nerve block was next attempted Apparently this provided excellent relief of pain The possibility of employing absolute alcohol was contemplated but was discarded temporarily in view of the proximity of the posterior tibial artery and vein A lumbar sympathetic nerve block was next performed in order to determine how much of the pain was mediated through sympathetic pathways there was none A program of weekly blocks of the medial plantar nerve with a local anesthetic was instituted Relief was very good and the intensity of the pain diminished considerably The possibility of injecting alcohol was again contemplated since it was feared that too frequent injections into the medial plantar nerve would eventually be traumatic and cause neuritis Therefore on introduction of the block needle during one procedure a direct contact with the nerve was obtained Pain was relieved with 1 cc of local anesthetic The needle was left in place and after 10 minutes 2 cc of absolute alcohol was instilled Pain relief was immediate and persisted for three days after which severe post alcoholic neuritis developed This was controlled by repeated blocks employing a long acting local anesthetic

This case is a good illustration of the value of frequent repeated local anesthetic blocks and makes one question the sagacity of employing absolute alcohol for peripheral nerve blocks

in the lower extremity therefore is involvement of the lumbosacral plexus by tumors arising from the uterus and its cervix the bladder the prostate and the rectosigmoid or tumors arising from the bony walls of the true pelvis Involvement may be in the form of pressure on the plexus or contiguous metastases Pain is usually referred all the way down to *the foot Not only pain but often weakness* of the lower extremities develops Pain may also be caused by the tumor pressing on the blood vessels to the leg thus interfering with its blood supply For this type of pain which develops secondary to pelvic conditions there is frequently an associated deep pelvic and sacral area of pain As was previously stated the nerve supply to the pelvic organs and the lower extremities are so intimately related that blocks applied to these nervous structures relieve pain in both the pelvis and the lower extremities Thus a lumbar sympathetic block such as an intrathecal alcohol injection to eliminate pain caused by masses in the pelvic cavity may also eliminate pain in the lower extremities

Pain may arise primarily from the lower extremity Tumors of bone may develop and cause severe pain and neuromas may give rise to pain What is more excision of a tumor or an extremity may leave a painful area or a phantom limb pain If the pain is localized in the foot or in the distal portions of the leg peripheral nerve blocks may work very effectively There should be a minimal loss of motor function with excellent pain relief However one may question the wisdom of instilling absolute alcohol into these nerves

diminish the convulsive seizures without excessive depression The excitement evoked by the situation might provoke the administration of a larger dose than necessary and give rise to a temporary state of barbiturate poisoning and its consequent respiratory and central nervous system depression Oxygen should be administered immediately and if the patient is apneic artificial respiration instituted If there is hypotension intravenous administration of fluids should be started and vasopressors employed (desoxyephedrine Neo synephrine or norepinephrine) Norepinephrine should be used only under extreme conditions when the patient does not respond to the other vasopressors

It must be emphasized that means for resuscitating the patient should be at hand whenever nerve blocks are to be performed A simple anesthesia bag and face mask attached to a controllable source of oxygen is sufficient for the administration of artificial respiration Intravenous fluids vasopressors and an ultra short acting barbiturate should be available for *immediate* injection

SUMMARY

Nerve blocks are not the final answer to the management of pain in malignancy They constitute only one of the many methods that may be used to make the pain less acute One should always be aware of their limitations but their value may be immeasurable when used judiciously in conjunction with other methods of treating pain

PREMEDICATION

The use of the ordinary premedicants like morphine and scopolamine in patients suffering from pain due to malignancy might appear superfluous These patients are often under such heavy doses of narcotics that further opiate administration is not necessary The short acting barbiturates are probably more effective *Phenothiazine derivatives like chlorpromazine* or phenergan when administered intravenously produce a tranquil sleeplike state from which the patient is easily aroused What is most impressive in the use of these drugs is that the patient becomes quite co operative It is always better to have a conscious patient when a block is being performed for by paying close attention to the patient s symptoms and the sensations that he feels as the needle is being placed the physician may be warned and able to prevent complications

REACTIONS TO LOCAL ANESTHETICS

Drug reactions may develop in a small percentage of cases True reactions may excite the central nervous system and cause convulsions, or depress it and produce unconsciousness Respiratory depression may also occur The reaction may include the cardiovascular system and cause a marked hypotension What is important however is that the developing reaction be recognized immediately and therapy instituted If convulsions occur an ultra short acting or a short acting barbiturate should be administered intravenously to

nant disease Occasionally however following amputation for malignant disease, there is return of pain in the arm or leg without painful metastases elsewhere In such a case, a painful neuroma may be the cause of the patient s distress A single attack on the remaining portion of the nerve is usually warranted—single because in most instances it will not suffice nor will repeated attacks for a neuroma Injection of alcohol or formaldehyde into the nerve does not prevent the neuronal regeneration to which the pain is attributed If the patient is in a terminal state, regeneration may not occur soon and hence a single resection of the neuroma (with insertion of a polyethylene tube over the end of the nerve or incasement of the nerve in a tunnel drilled in the bone) is warranted If there are no other signs of metastasis and the pain recurs posterior root section may be attempted

When there are already metastases from a malignant disease of an extremity making amputation of the painful limb appear unwarranted peripheral nerve section is not indicated because overlap of sensory distributions would make section of numerous nerves necessary with considerable motor deficit as well as sensory loss Instead spinothalamic tractotomy would probably be indicated (see p 97)

CRANIAL NERVE SECTION

When pain arises from carcinoma in the distribution of the cranial sensory nerves peripheral section may

CHAPTER 3

Neurosurgical Aspects of Pain Management

NEUROSURGICAL TECHNICS for the relief of pain vary from peripheral nerve section to destructive procedures on the brain Each has some drawbacks aside from the necessity of an operation but the help and relief of pain can be so great that consideration should be given to such procedures In order that the operation not be rendered unduly hazardous neurosurgical attack should be considered before debility and addiction are advanced The technics described in the following pages range from the simplest attack on the peripheral nervous system to the most complex procedures on the central nervous system

PERIPHERAL NERVE SECTION

There is little use for nerve section in the extremities as an independent procedure the nerves may be cut in the course of amputation for sarcoma of the bone but not for most terminal or inoperable malig

more common to use nerve root section or section of the descending pain pathways in the medulla ob longata

NERVE ROOT SECTION

By attacking the peripheral and cranial nerves near their origins or attachments to the brain and spinal cord it is possible to produce sensory loss without motor involvement

Posterior (dorsal) root section for the *peripheral nerve* elements entails laminectomy for any area below the head A midline incision is made over the required number of spinous processes (One should remember that any one peripheral skin area is supplied by at least three and sometimes more posterior roots) The muscles and ligaments are detached from the spinous processes and laminae and the bony arches removed to allow access to the spinal dura mater This is in cised longitudinally and the dorsal roots isolated and cut It is necessary to spare any large vessels on these roots especially on the 3d and 4th cervical the 4th and 7th thoracic and the 1st lumbar roots for these large radicular vessels may be the chief source of supply for the spinal cord especially in the thoracic area If these radicular vessels are occluded softening of the adjacent spinal cord may result The dura mater is then closed before suturing the muscles and skin The operation is done with the patient prone (some times sitting for cervical root section) and it can be performed under local anesthesia although general anesthesia is usually more comfortable for a patient

be undertaken but the possibility of regeneration in three to four months must be weighed against the probable survival time The forehead and anterior scalp are supplied by the ophthalmic division (supraorbital branch) of the trigeminal nerve This nerve can be avulsed readily under local anesthesia through an incision just above or just below the eyebrow The resulting area of anesthesia can be extended by similar section of scalp nerves from the upper cervical roots and plexus (greater and lesser auricular nerves greater and lesser occipital nerves) Lesions of the side of the nose upper cheek and lip can be denervated by avulsion of the infraorbital nerve (branch of the maxillary division of the trigeminal nerve) Incision is made under local anesthesia in the mucosa over the first bicuspid area and the nerve grasped as it leaves the infraorbital canal Sensation in the lower jaw (except for the lateral aspect of the skin overlying the middle of the ramus which is innervated by the upper cervical roots) can be abolished by section of the mandibular nerve as it enters the notch An incision is made in a skin crease over the mandibular ramus and a small burr hole made through the bone over the mandibular canal The lower teeth gums and chin can thus be anesthetized

No other sensory cranial nerve can be readily approached for section As a matter of practice it is relatively rare that trigeminal nerve branch section is done for pain in the face, for the local approaches cited above are almost always debarred by the local cancer for which relief is required It is hence much

and nearby zones can be stopped by section of the trigeminal root an operation which has become standardized in the treatment of trigeminal neuralgia Root section has the advantage that regeneration does not occur (as with peripheral nerve section) and the operation is done in a region usually remote from the carcinoma

Under local or general anesthesia with the patient seated a vertical incision is made in front of the ear just above the zygoma After separating the fibers of the temporal muscle a burr hole is made in the thin temporal bone and enlarged to a diameter of 5 cm (2 in) The temporal dura mater is lifted from the base of the skull allowing access to the middle meningeal artery which is ligated coagulated or compressed and cut Medial and slightly forward the mandibular division of the trigeminal nerve is found The dura mater is opened behind this division and the sensory root of the trigeminal nerve cut or avulsed The temporal muscle and skin are closed in layers Ordinarily patients in the sixties and seventies who have this operation for tic douloureux can be up in a day or two even though they are usually debilitated and the same is true of carcinoma patients The death rate is less than 1 per cent Facial paralysis or weakness attributed to stretching of a branch of this nerve is quite rare (less than 2 per cent) and permanent paralysis is almost unheard of The motor branch of the trigeminal nerve is sometimes cut producing paralysis of the muscles of mastication on the same side but this rarely causes any distress in chewing or talk

with intractable pain The surgical trauma is dependent on the extent of the desired denervation, certainly enough exposure for section of the roots of three spinal nerves can be obtained without loss of so much blood as to require transfusion The mortality should be no more than that of laminectomy for disk protrusion (less than ½ per cent), and when the patient recovers from the anesthesia there should be no difficulty with bowels or bladder unless sacral roots have been cut Convalescence takes from 7 to 10 days depending on the general condition of the patient There is no motor loss from such a procedure and the loss of sensation is for all modalities

Unfortunately such an operation is of limited usefulness for most visceral pain cannot be eliminated by posterior root section unless very extensive However, just as angina pectoris may be overcome by section of the upper four or five thoracic roots pain of malignant disease of the chest with parietal pleural invasion can be similarly eliminated Carcinoma involving the upper cervical plexus can also be handled in this manner However section of the posterior roots contributing to the brachial plexus may not alleviate pain for reasons which are not clear and even if the pain is alleviated the limb is useless for without sensation effective motor function is impossible However, when there has been amputation for malignant disease posterior rhizotomy may be very effective

On the other hand *cranial sensory root* section is one of the most useful operations for the relief of intractable pain Such distress anywhere in the face

closed In most instances the patient can be up in a day or two, with very little headache Sometimes ataxia of the ipsilateral limbs can result from retraction of the cerebellum but this is transient Rarely there may be vertigo for a week or two from disturbance of the equilibratory mechanism Mortality ranges up to 5 per cent depending on the status of the patient (usually poor with malignancy of the throat) In itself glossopharyngeal nerve section causes no detectable motor weakness in swallowing and the anesthesia of half of the pharynx is rarely disturbing to the patient During the operation there is usually a transient elevation of blood pressure from section of the nerve roots (carrying the impulses from the carotid sinus) but this rarely outlasts the operation and even then lasts not more than a day or two Bilateral glossopharyngeal root section can be carried out at the same sitting without much added risk—and again swallowing is not impeded Indeed patients unable to swallow because of pain before surgery may be able to do so postoperatively

In a very rare case pain in the ear due to cancer may not be relieved by glossopharyngeal upper vagal or trigeminal root section The nervus intermedius a sensory branch of the 7th nerve may be involved This nerve runs as a separate filament on the facial nerve and is usually hidden by the 8th It can be cut by an approach similar to that for the 9th nerve (or posterior approach to the 5th nerve root) but if it is suspected that pain may be due to this nerve the operation should be done under local anesthesia or

ing Anesthesia of the cornea causes some concern especially if facial paralysis is already present (for example with parotid gland tumor) Suture of the lids to narrow the palpebral fissure may be carried out and certainly an eye shield should be used with careful and frequent inspection of the eye to insure absence of any foreign body It is sometimes possible to cut only the lower two thirds of the fibers of the root to preserve innervation of the eye and forehead if these parts are not involved in the pain

Relief of pain in the throat (and sometimes the middle ear) can be accomplished by section of the glossopharyngeal root (9th cranial nerve) This root is approached by a vertical incision medial to the mastoid bone usually under general anesthesia and with the patient lying in a face rest in the horizontal position Local anesthesia can be used if desired The nerve roots from the 7th to the 9th nerves are exposed by removing the bone medial to the mastoid process opening the dura mater and retracting the cerebellum to the opposite side The facial and auditory nerves (and often a separate nervus intermedius) can be seen entering the internal auditory meatus The 9th nerve arises by a series of rootlets from the lateral aspect of the medulla oblongata and these are cut separately It is common practice to include the first one or two rootlets of the vagus nerve as well for these may carry some sensation from the pharynx Extensive vagus section is to be avoided lest paralysis of the vocal cords and difficulty in swallowing arise Following root section the nuchal muscles and skin are

anesthesia, the cut can be made deeper or more dorsal as the case may indicate The dura mater is then closed followed by layer closure of muscles fasciae and skin Because of the interscapular location of the incision motion of the patient s arms is usually restricted for 5–10 days If the section is made at the 2d thoracic level such restriction may not be needed At the end of this time the patient can be allowed up

The immediate loss of pain perception usually drops a segment or two in the first few days or weeks after operation For this reason some neurosurgeons prefer to do the operation under general anesthesia and make a maximum cut immediately The complications include death (usually less than 1 per cent at this operative site) temporary weakness or paralysis of the ipsilateral lower extremity (5–10 per cent) and loss of control of the sphincters Urinary control may be interfered with in up to 5 per cent of the patients bowel control in fewer patients Touch and position sense are left undisturbed Often the relief of pain is so sufficient that the patient begins to complain of pain on the opposite side present but of minor degree before operation (as in inoperable carcinoma of the uterus or rectum) It is then possible and proper to reopen the incision and make a similar cut on the intact side for relief of the residual pain When there is midline or bilateral pain both cuts can be made at the same operation but they are then made at least one segment apart on the opposing sides so as not to impair the circulation of the spinal cord When ever possible a week s interval between the two cuts

with such anesthesia that the patient can be awakened at the time of nerve section, to allow mild electrical stimulation of the nerve If such stimulation reproduces the pain then the nerve can be sectioned

SPINOTHALAMIC CHORDOTOMY

Perhaps the most useful operation for relief of pain below the shoulder girdle is section of the pain pathways in the spinothalamic tract which runs in the anterolateral portion of the spinal cord When this tract is cut in the upper thoracic region there is usually good somatic and visceral analgesia from the lower thoracic region caudally on the side opposite to the cut

Under local or general anesthesia with the patient prone laminectomy is done at the 2d or 3d thoracic vertebral level Usually the entire neural arch of one or two vertebrae is removed although there is a recent trend toward hemilaminectomy The dura mater is opened to allow access to the dentate ligaments which hold the spinal cord to the interior of the dura mater A pair of ligaments is cut one is grasped and the cord is rotated Then a sharp blade is inserted at the attachment of the dentate ligament to the cord and virtually the entire anterolateral quadrant of the cord is cut If the patient's condition warrants the operation can be done under local anesthesia or under a short lasting general anesthetic so that the patient can be awakened for testing of the level of sensory loss after the incision is made If there is insufficient

one to two segments) Cervical chordotomy can be accompanied by section of the upper three or four posterior roots on each side, to extend the level of anesthesia and also to help make the convalescence almost painless (since the incision is thus denervated) There is no impairment of healing by such sensory section Bilateral cervical chordotomies may be done often cervical chordotomy on one side may be ac companied by or followed by thoracic section on the other after a week or two This is believed to minimize sphincter and motor weakness With bilateral chordotomies there may be a frightening drop in blood pressure for some days after operation but this is transient and can be combated in the postoperative period by pressor drugs such as methamphetamine, still later, an abdominal binder and leg wrappings can be used as temporary measures while the patient adjusts to the vasomotor instability so like that of bilateral thoracolumbar sympathectomies

SPINOTHALAMIC TRACTOTOMY

The spinothalamic tract can also be cut anywhere from the spinal cord to the thalamus In the lower portion of the medulla oblongata the pain pathways lie laterally placed and can be cut by an incision in the lateral aspect of the medulla The pyramidal tracts are placed ventrally and there is little danger of in jury to them The difficulties come from the pial vessels on the surface of the medulla and from the nearby descending root of the trigeminal nerve How

is best for this lowers the weakness which follows operation from 10 to 5 per cent and reduces the bladder complications of bilateral one stage procedures by half Permanent sphincter paralysis may result and necessitate an indwelling catheter, with the risk of infection This is not an importanct factor if the bladder and ureters have already been involved in the *malignant disease process*

Failure to obtain relief of pain from a well planned unilateral operation may be overcome by cutting the second side in rare instances Lack of success is attributed to failure of crossing of the secondary pain pathways in the spinal cord—an anomaly which cannot be anticipated and which must be quite uncommon

Spinothalamic chordotomy is also used to give relief of pain in cervical and upper thoracic segments (for example for pain in the upper extremity as with superior pulmonary sulcus tumor) The cut is then made at the 1st or 2d cervical level in a procedure which differs from the thoracic procedure only in minutiae The exposure is more time consuming and somewhat more hazardous (3–5 per cent mortality) and there is less assurance of success, for the sensory level may drop in spite of what appears to be an adequate section Nevertheless it can be very useful and is sometimes preferred to thoracic section even for abdominal pain By using the higher level any unusual anatomic peculiarity may be thwarted (for example crossing of sensory fibers five to six segments above entry into the spinal cord instead of the usual

caudal to the inferior angle of the 4th ventricle (obex) and 6 mm lateral to the midline going as deep as 4 mm Cerebellar ataxia is rarely a problem with such a caudal section Pain and temperature sense are lost on the face (and often in the throat and ear as well) Touch is preserved so the dangers of corneal damage are greatly minimized There is no interference with the muscles of mastication which may occur with posterior trigeminal root section

The spinothalamic tract then burrows into the depths of the medulla and pons Pontine attack by electrocoagulation has been attempted but is not actively used at present The tract comes close to the surface again in the mesencephalon here it forms part of the lateral lemniscus along with secondary trigeminal and other facial sensory pathways The operation involves making a large occipital flap elevation of the occipital lobe of the brain section of the tentorium and visualization of the lateral aspect of the mesencephalon A 5 mm incision is made across the brachium of the inferior colliculus ending at the inferior margin of the superior colliculus Operative mortality reportedly ranges from zero to 80 per cent The analgesia produced tends to fade and there has been considerable paresthesia in some patients There is no disturbance of micturition and no risk of injury to corticospinal pathways This operation should be considered an experimental one but it bears consideration in certain cases of carcinoma of the pharyngeal region where pain may be carried by the vagus nerve not amenable to nerve root section on both sides because

ever if this trigeminal root is partly cut the small zone of pain loss on the face will not prove to be very bothersome The operation is more dangerous than cervical chordotomy (10–30 per cent mortality in different series) and is more difficult to carry out but it may give a very satisfactory loss of pain in the upper extremity and nearby neck

Through a midline occipitonuchal incision the occipital bone and first cervical lamina are exposed, the latter is removed and bone around the foramen magnum removed to allow opening the dura mater and access to the lower portion of the medulla oblongata *Just anterior to the line of emergence of the rootlets* of the spinal accessory nerve a cut is made 6 mm deep and 4 mm dorsally Testing of sensation can be carried out if the operation is done under local anesthesia The lower portion of the dura mater is usually closed and the muscles and skin closed in layers Some ataxia may follow the operation The level of analgesia may drop with this procedure as with all tractotomies since some of the immediately postoperative sensory loss can be attributed to swelling and pressure on adjacent fibers Bilateral medullary tractotomy has been fatal (presumably due to interference with vital centers in the bulb) and it is not done in one stage If the neck is supported with a firm dressing the patient can be allowed up as soon as headache permits

The same approach is used for section of the descending tract of the trigeminal nerve This has a constant location and can be cut by an incision 6 mm

procedure is time consuming but thus far neither hazardous nor very painful If all is well an electrolytic current is passed in to cause a small area of necrosis in the spinothalamic tract The hazards of improper needle placement are obvious the wrong locus may be damaged so that no anesthesia results or nearby structures may be damaged with unwanted effects However the accuracy of the lesion placement in the hands of the more experienced operators is sometimes astounding and such lesions may give relief of pain when nothing else can How long the anesthesia will last and what paresthesias may result are questions that cannot be answered as yet Obviously the same technic can be used to cause lesions in the end station for pain in the posterolateral nucleus of the thalamus This is a large area and stereotaxic lesions may miss vital areas

The radiations from the thalamus toward the cerebral cortex in the posterior limb of the internal capsule could also be attacked but the proximity of voluntary motor pathways and other sensory radiations have hindered such a procedure Furthermore there is adequate evidence that cortical ablations do not cause analgesia so it is unlikely that attack here is likely to arouse interest

FRONTAL LEUKOTOMY

The use of destructive lesions of the frontal white matter for alleviation of pain arose as an incidental finding in patients with lobotomy done for mental illness Actually there is no interference with primary

of the vocal cord and swallowing paralysis as well as respiratory complications

STEREOTAXIC LESIONS

The same locus in the mesencephalon can be reached by a needle inserted from the convexity of the skull and the tract destroyed by an electrocoagulation current *Accurate placement of such an electrode* is dependent on a stereotactic instrument—a device for locating certain fixed landmarks in the brain and for placing the needle a designated distance from such a landmark The wide range of head and brain size in man makes this task far more complex and difficult than in laboratory animals with less variable skull sizes (young adult monkeys adult cats) There are a few centers in the United States and Europe where such instruments are in use, but in almost all centers patients are accepted only on an investigative basis In brief the procedures usually entail filling of the ventricular system of the brain with air and obtaining roentgen films of the ventricular system with a superimposed co ordinate grid A metal frame is affixed to the skull in a manner permitting exact reapplication at a future time A drill hole is made through the skull in a location calculated to permit insertion of the needle to the desired site Repeated co ordinate and grid studies are carried out usually basing the co ordinates on a fixed neuroanatomic structure such as the pineal body or the posterior commissure nearby A needle is inserted brain waves are usually recorded and stimulation at the needle tip is carried out The

pain with diminished psychological upset In the few patients treated in this manner the results have been encouraging within the short follow up period

A number of technics have been used for lobotomy perhaps the safest is the following Under local or general anesthesia the shaved scalp is infiltrated with procaine in line with the pupil of the eye Incision is then made parallel to the long axis of the head (para sagittally) in the frontal region, to allow exposure of the coronal suture A trephine opening is made just anterior to the suture line and the dura mater opened Through a stab wound in the cortex a ventricular needle is inserted toward the posterior rim of the roof of the orbit If the ventricle is encountered the needle is angled further anteriorly With retractor and suc tion cautery the white matter of the frontal lobe is incised down to the gray matter of the orbital cortex medially and laterally to the corresponding cortical gray matter A piece of Gelfoam containing air or a few drops of opaque oil is inserted to mark the plane of section in x ray films and the wound closed in layers after replacing the trephine bone button for cosmetic purposes The contralateral side may be cut in a similar manner or only one side done

It may be worth while to open the other side making sure to have a drill hole through the bone but ton and to coagulate the brain surface underneath before closing the wound Thus the basic opening is ready for a future second stage procedure perhaps an open lobotomy or if desired a spinal needle can be inserted into the white matter (with x ray control)

pain pathways, the patient can still feel pain arising from within or superimposed from the outside However, in the lobotomized patient the reaction to such pain is far different from the reaction in the normal person Usually the patient makes no spontaneous complaint of pain and is not preoccupied with it If pain does occur or is evoked the reaction is less intense and does not concern the patient If narcotic addiction has been present dependency is relieved Strangely enough after bifrontal leukotomy withdrawal symptoms from abrupt cessation of morphine administration do not occur The drawback to frontal leukotomy is the mental change produced in the patient the predominant features are impaired judgment and deterioration in behavior Incontinence disorientation and apathy are commonly seen Because of these symptoms unilateral leukotomy has been proposed to diminish the undesirable side effects When effective the mental changes are much less marked The decrease in spontaneous speech and the flattening or inappropriateness of emotional responses seen with unilateral operation are much less disturbing than with bilateral operation and pain and suffering may be reduced to a tolerable level When the patient survives more than four to six months pain complaints are likely to recur after unilateral leukotomy If suffering is again intense operation on the second side can always be carried out although at the price of severe psychological change especially in the early postoperative period Section of only medial portions of the frontal white matter has also been aimed at relief of

MISCELLANEOUS PROCEDURES FOR RELIEF OF PAIN

Intrathecal Alcohol and Phenol

In patients with radicular and segmental pain corresponding analgesia may be obtained by injection of 95 per cent or absolute alcohol into the subarachnoid space The technic is described in Chapter II, in brief spinal puncture is done at the level desired with the roots to be blocked uppermost A small amount of alcohol is injected slowly and it rises to the dorsal roots Heavy phenol solution can be similarly used with the painful side lowermost the chemical falls to the bottom of the subarachnoid space These procedures are valuable in patients who are in too poor condition for chordotomy and have short life expectancy Thoracic injections carry risk of transverse myelitis and lumbar injections may lead to weakness of the legs and sphincter incontinence

Sympathectomy

There is little doubt that in some patients pain fibers run in the sympathetic chain and denervation by removal of these fibers may give relief of certain types of pain Such visceral denervations are only temporarily effective in treatment of pain of malignant disease (for example splanchnicectomy for relief of carcinoma of the pancreas) for the tumor spreads to involve somatic nerves as well Chordotomy is much

and procaine or alcohol can be injected to see what effect mechanical section of the frontal white matter can have on pain and suffering Alternatively small burr holes can be made bilaterally and the dura mater and brain surface prepared for injections several days later Graded injections can thereafter be carried out at leisure and the results of permanent white matter destruction approximated These holes could also be used for graded destruction of the medial quadrants by electrolytic currents passed through needle elec trodes (insulated except at their tips) For any of these "blind" procedures it is convenient to fill the ventricles with air or oxygen and to place the needles anterior to the ventricles as checked by x ray

The operative mortality from frontal lobotomy should be less than 2 per cent The danger of post-operative convulsions is about 10 per cent although such seizures are readily controlled by standard anti-convulsant medication

In general frontal leukotomy should be reserved for pain which experience has shown does not respond to less radical procedures The operation is considered strongly when the malignant process is a disfiguring one and is accompanied by much mental anguish It is less demanding on the patient s resistance than say rhizotomy or chordotomy but ease of performing the operation should not blind one to the mental changes Most neurosurgeons do not believe that lobotomy by transorbital route ("ice pick" operation) is of much value in intractable pain

do not develop reoperation is advised Complications are few and are principally those of the neurosurgical procedure (for instance blood clot) they can usually be handled quite effectively

The contraindications to hypophysectomy for breast carcinoma include known metastases to the brain Metastases here in the presence of a known source of active cancer are ordinarily not treated surgically since life expectancy is very short On very rare occasions when headache nausea and vomiting are exceedingly troublesome decompression by standard neurosurgical technics may be warranted When the primary carcinoma has apparently been eradicated and signs of intracranial disorder appear operation should be considered Long delayed metastases from hypernephroma and breast cancer are not unknown and if as is sometimes the case the metastasis is solitary operation may be lifesaving Furthermore the intracranial lesion may not be related to the original cancer The same considerations apply to tumors of the spinal cord for benign tumors of the spinal cord may become evident only after some carcinoma has been apparently removed One should not believe that the spinal lesion is necessarily metastatic without making further investigation Because spinal metastases are so rapidly productive of paraplegia—and this does not imply imminent death—most neurosurgeons believe in decompressive laminectomy even for known metastatic disease to the spine in the hope of delaying the immobility and nursing problems of paraplegia

more effective in such cases However, as a temporary measure for patients in poor physical condition, para vertebral injections of alcohol may damage the sym pathetic chains enough to give considerable relief The technics are described in Chapter II

Hypophysectomy

There has been considerable success reported in alleviating pain of metastases and in improving the patient s condition generally from hypophysectomy for breast carcinoma but the operation appears to have little indication in other types of malignant dis ease in which trials have been made There appears to be less postoperative distress to the patient than after adrenalectomy To be effective, all of the hypo physeal anterior lobe must be removed

A standard right frontal craniotomy approach can be used, with more room obtained by continuous spinal drainage during the procedure The stalk of the hypo physis is clipped and cut the diaphragma sellae in cised and the gland evacuated by curettage To help insure destruction of small residues of gland Zenker s solution is instilled into the cavity The mortality rate is 3–5 per cent but the postoperative course is usually smooth No particular endocrine therapy need be given preoperatively but maintenance doses of cortisone are given after operation Effectiveness of removal can usually be measured by quantitating the responses to cortisone If the signs of hypophyseal inadequacy

on the sympathetic nervous system In malignancy this is rarely effective unless the cancer is still restricted within the capsule of the viscus When there has been spread spinothalamic tractotomy should be employed Unilateral section may be sufficient when the pain is unilateral

THORAX

The pain of breast and lung carcinomas may be the most difficult to handle It is frequently bilateral and involves the upper extremities When the pain is unilateral and the upper extremity is weak, swollen and useless posterior root section may be performed although a long laminectomy may be needed to de nervate the arm completely Otherwise chordotomy at the 1st cervical level or section of the spinothalamic tract in the medulla oblongata may give a satisfactory level of anesthesia In cervical chordotomies bilateral section of the posterior roots makes convalescence from the operation more pleasant without incapacitating the patient Although bilateral cervical chordotomy can be done at one sitting two stages are preferable Unfortunately the operation may not always give lasting relief from pain In this event, unilateral frontal leukotomy or bilateral medial frontal quadrant section may be quite effective

NECK

Pain restricted to the region between the ear and the clavicle (as in carcinoma of the submaxillary area)

NEUROSURGICAL ASPECTS OF PAIN BY REGION

Pelvis

Carcinomas in the pelvis may lead to pain in the low back, buttocks legs lower abdomen and pelvis Anterolateral chordotomy is the treatment of choice especially when the pain is unilateral The family should be aware of the frequent postoperative complaint of contralateral pain which probably exists before operation but is unmasked by the relief of the major pain Second stage operation can be done through the same incision in five to eight days Such staged bilateral operations are less likely to produce sphincter disturbance than simultaneous section of both tracts The major complications are weakness paresthesias of the analgesic legs sphincter disturbance and temporary hypotension When the carcinoma *has led to colostomy and bladder drainage, and* the pain is limited to the penis perineum and saddle area the patient may well be in too poor condition for surgery and in such a patient the injection of alcohol into the lumbosacral subarachnoid space may suffice to make the pain disappear In rare instances there may be persisting pain often of a burning nature following any procedure for relief of pain even with good analgesia for external pain When this occurs leukotomy of some sort is indicated

Upper Abdomen

Pain from nonmalignant disease of the pancreas liver stomach etc may often be relieved by attack

CHAPTER 4

Humoral and Chemical Palliation of Malignancy

In malignancy the use of agents or procedures to alter the humoral balance has one primary objective—to produce an environment unfavorable to the growth and development of the neoplasm In favorable circumstances a decrease in the size of the primary or secondary malignancy is temporarily possible Unfortunately although many hormones are available as pure chemicals and although complete surgical removal of an endocrine gland is possible the effects are not simple For example the results of the administration of an estrogen are not confined to the production of a single phenomenon The direct effects of any hormone are multiple and complex and the magnitude and implications of these effects are compounded by the complexities and interrelationships of the entire endocrine system The stability of the internal environment rests on a continually fluctuating and dynamic system of balances If we upset this equilibrium by introducing a massive weight of one hormone or by

may be handled effectively by section of the first four or five cervical posterior roots When the cervical pain is associated with arm or chest pain spinothalamic tractotomy is added When suffering is great and there is fear of strangulation or death from hemor rhage leukotomy may be chosen as the first procedure

FACE AND THROAT

Section of the trigeminal glossopharyngeal and up per vagal nerve roots is usually adequate to relieve unilateral pain in the face and throat Section of the trigeminal pathways in the medulla oblongata may be useful when combined nerve root sections are needed or when access to the middle fossa is pro hibited by a malignant lesion in the vicinity When there is considerable psychic disturbance, as with dis figuring lesions leukotomy may be performed first in such a case apathy may be a desirable goal

SUMMARY

Most neurosurgical procedures for relief of pain for terminal carcinoma require a major operation and can not be done if the patient is in too poor condition Because such operative relief of pain may be well worth while consideration of such procedures should not be too long delayed In general operative relief of pain should be considered when the patients pain is no longer relieved by codeine and when life ex pectancy is two months or more

extremely ill patient hauled from town to town or spend his last few pennies or those of his relatives attempting to find the panacea Some of these alleged "cures" are promoted by well intentioned individuals with inadequate knowledge of the natural course of the disease, but all too frequently an utterly worthless agent receives unwarranted acceptance merely because it is sponsored by someone who has achieved fame in other fields Fortunately the National Research Council has established a Committee on Cancer Diagnosis and Therapy, which is willing to screen any "cancer cure" and at the same time protects the interests of the inventor The drugs are distributed to expert and experienced investigators who report their clinical and scientific observations to this Committee A physician can obtain information on any of these so called cures from the National Research Council Committee on Cancer Diagnosis and Therapy 2101 Constitution Avenue Washington 25 D C

The discussion of procedures and therapy in this chapter is limited to those situations where there is no possibility that the malignancy can be eradicated by surgery or radiation Therapy with hormones or chemicals must however be considered in relation to the other technics available for the management of malignancy It is our purpose to outline the role of the internist as a member of a team all of whom are contributing toward the alleviation of the pain and suffering associated with cancer The discussion is divided into two general sections (*a*) a description of the clinical management of the more common types

cutting off the source of another the resulting im balance produces widespread and varied effects on the host Thus, we can never produce only the single desired effect by such technics we may partially achieve our goal but at the price of other derange ments

The introduction of specific chemical agents in the management of malignancy must be considered a cal culated risk The ideal agent is one which exerts the desired effect on the target cell or organ without pro ducing any other pharmacologic effect There is no chemotherapeutic agent which meets this requirement At best we hope to depress a malignant condition in the host by substituting the lesser toxicity (we trust) of the chemotherapy The foregoing should not be interpreted as negative or discouraging statements be cause therapy with hormones and chemical agents has demonstrated that a variety of tumors are not entirely autonomous in their growth and that they can be influenced profoundly albeit temporarily by these agents When it is impossible to cut out or burn out a tumor chemotherapy provides a valuable third approach

A physician caring for a patient with incurable metastatic cancer is frequently besieged by well mean ing relatives and friends who suggest certain forms of therapy that have received great notoriety through the lay press advertisements or hearsay It is the responsi bility of the attending physician to make a decision as to whether it is worth while to try any of these agents There is nothing much more tragic than having an

extremely ill patient hauled from town to town or spend his last few pennies or those of his relatives attempting to find the panacea Some of these alleged "cures" are promoted by well intentioned individuals with inadequate knowledge of the natural course of the disease but all too frequently, an utterly worthless agent receives unwarranted acceptance merely because it is sponsored by someone who has achieved fame in other fields Fortunately the National Research Council has established a Committee on Cancer Diagnosis and Therapy which is willing to screen any "cancer cure" and at the same time protects the interests of the inventor The drugs are distributed to expert and experienced investigators who report their clinical and scientific observations to this Committee A physician can obtain information on any of these so called "cures" from the National Research Council Committee on Cancer Diagnosis and Therapy 2101 Constitution Avenue, Washington 25 D C

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of malignancy that may be influenced favorably by alterations in the humoral balance or by chemo therapy, and (*b*) brief descriptions of some of the more important pharmacologic characteristics of the agents used in therapy

CLINICAL MANAGEMENT OF MALIGNANCY

Cancer of the Female Breast

Unfortunately one of the most common malig nancies cancer of the breast is cured by definitive therapy in less than half the cases Because of the nature of the spread of the disease into the viscera and bone great disability and pain ensue Character istically metastatic cancer of the breast is a slow killer but produces increasing suffering that may last for many months or years Any procedure that temporarily rehabilitates such people seems justifiable It is fortu nate that many cancers of the breast do not show complete autonomy of growth and certain specific forms of therapy will temporarily alter the course of the disease markedly Although these procedures are of only temporary benefit there is under the best of circumstances worth while rehabilitation of previously bedridden patients for as long as two or three years

Estrogen therapy —Pharmacologic doses of estro gen cause tumor regression in about 50 per cent of patients when the primary tumor develops in a patient ten or more years postmenopausal Dramatic regres sion of soft tissue metastases occurs in some patients Osteolytic metastases may also show recalcification

although this is not demonstrable by roentgenography for several months Along with tumor regression pain relief improvement in general health and control of other symptoms due to the localization of the metastases can be expected to occur

On the other hand some patients may show an apparent augmentation of tumor growth during estrogen therapy This is more common in the pre or immediately postmenopausal patient It is therefore of the utmost importance that the patient be under very close observation for the first few weeks of therapy However, rather acute swelling and increased pain in the soft tissue lesions during the first two weeks of therapy may precede a period of major regression of the tumor and so it is wise to continue therapy for at least one month before concluding that the estrogen is producing an augmentation Regressions may continue under this therapy for from four months to several years In general an estrogen produced regression is more complete and of longer duration than an androgen produced regression

The mechanism by which estrogens produce temporary regression is not understood It has been postulated that the common tumor of the breast in the postmenopausal woman consists mainly of cells that cannot grow in a substrate containing estrogens However malignant cells that require estrogen for growth are present in small number Thus administration of estrogen depresses the dominant cells and thereby the total tumor mass shrinks In time however the tumor reappears in the same site and it is not affected by

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of not being able to withdraw the estrogen abruptly in case of augmentation of tumor growth or hypercalcemia

The physiologic actions of estrogens must be borne in mind when administering large doses of the hormone Withdrawal bleeding even in the aged patient is the rule Regrowth of atrophic uterine fibroids may occur and reactivation of chronic cystic mastitis is common We have observed hematometra in two aged patients with stenosis of the cervical os Since interrupted therapy causes frequent episodes of uterine bleeding it is advisable to give continuous therapy until bleeding occurs and then omit the drug until bleeding has stopped (If bleeding does not stop in 10 days 100 mg progesterone intramuscularly may be given for 5 or 6 days) Therapy should be continued until evidence of progression or augmentation develops or until all clinical evidence of metastatic disease has disappeared (a rare situation) Treatment may be reinstituted when the disease becomes reactivated and a second third or fourth regression may occasionally be produced Usually however the tumor becomes less and less responsive to the hormone

Estrogens given to the aged patient for metastatic cancer of the breast not infrequently produce other benefits such as revitalization of the atrophic skin and mucous membranes and reappearance of subcutaneous fat, producing improved tissue turgor On the other hand estrogens in high doses produce sodium retention and congestive heart failure may develop unless proper cardiac management is instituted Also patients

continuing the estrogen therapy This hypothesis is supported by the fact that it is not uncommon to ob serve a secondary tumor regression on cessation of estrogen therapy in an individual who has previously responded favorably and then relapsed while still receiving estrogen Another possible explanation of the depressing effect of estrogen on cancer of the breast is that high doses of the hormone depress the hypo physis which produces certain hormones favorable to tumor growth (somatotropin?, prolactin?)

Regression of metastatic cancer of the breast has been reported with doses of from 3 to 500 mg di ethylstilbestrol a day It is probable that 15 mg daily will accomplish as much as larger doses and less than this amount may not be sufficient in most cases The estrogen is given orally in three divided doses after meals About 25 per cent of the patients complain of nausea during the first week of therapy but only rarely is a patient unable to tolerate the drug Anti emetic drugs may be of help in some cases If the patient is unable to tolerate this dose of diethylstil bestrol by mouth she will probably experience the same discomfort with the equivalent dose of other estrogens given orally although ethinyl estradiol 3 mg or conjugated estrogenic substances (for instance Premarin) 30 mg may be substituted If oral medica tion is not tolerated, the intramuscular administration of estradiol benzoate or dipropionate, 5 mg twice a week may be substituted The long acting estrogens are less satisfactory because of troublesome prolonged uterine bleeding on omission and the added hazard

been doing the patient a favor by giving androgens because of the emotional impact produced by mas culinization On the other hand, the euphoria and in creased libido seem to be welcomed by other patients Before embarking on androgen therapy it is wise for the physician to size up his patient in order to predict the psychological reaction to masculinization We have seen many patients who bitterly resented the results of androgen therapy

Androgens are most conveniently given in the form of methyl testosterone 25 mg four times a day by mouth Nausea sometimes occurs with this dose in which case 100 mg testosterone propionate in oil may be given three times a week intramuscularly The long acting intramuscular preparations carry with them the same objections as the long acting estrogens and are even more hazardous because of the greater frequency of hypercalcemia during the use of androgens The so called "weaker androgens are not recommended since it is now apparent that the palliative effect depends on the androgenicity of the product The tumor depressing effect of androgens is not under stood it may be due to neutralization of estrogens or to depression of the anterior hypophyseal hormones Androgens should be continued for a minimum of two months before being discarded as a means of palliation unless psychological or clinical contraindi cations are apparent The drug is highly anabolic, and most patients have an increased appetite feel stronger and develop *an improved hemogram* or even poly cythemia Because of marked sodium retention re

with extensive osteolytic metastases may develop dangerous hypercalcemia during estrogen therapy The sudden development of nausea and lethargy should be considered as signs of hypercalcemia until disproved by normal serum calcium values or negative Sulkowitch reaction of the urine Radiation has been used in conjunction with similar doses of estrogens in the younger age group by Dr Ira Nathanson who felt that estrogens seemed to increase the effectiveness of radiation therapy

ANDROGEN THERAPY —Androgens in large virilizing doses produce temporary regression in about 20 per cent of patients with metastatic cancer of the female breast The regression of the soft tissues is usually not so definitive as with estrogens but is effective in the same proportion in all age groups Recalcification of osteolytic metastases is demonstrable sooner than that produced by estrogens and pain from osseous lesions is more effectively relieved It is of interest that pain relief occurs in about 65 per cent of the patients suffering with osteolytic metastases although recalcification of the lesions is demonstrable in only about 16 per cent It is not uncommon for the patient to experience an increase in pain during the first two weeks of therapy and later obtain gratifying pain relief

The major objection to the use of androgens are the disfiguring effects of masculinization together with distortion of the psyche Even in patients receiving considerable pain relief and temporary tumor regression it is sometimes doubtful that the physician has

been doing the patient a favor by giving androgens because of the emotional impact produced by masculinization On the other hand, the euphoria and increased libido seem to be welcomed by other patients Before embarking on androgen therapy it is wise for the physician to size up his patient in order to predict the psychological reaction to masculinization We have seen many patients who bitterly resented the results of androgen therapy

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striction of this element is frequently necessary For this reason it is usually unwise to use androgens in the presence of considerable ascites pleural effusion borderline congestive failure or severe lymph edema

OOPHORECTOMY —Although oophorectomy was reported to be of value in far advanced cancer of the breast in the last part of the nineteenth century it has not been used extensively as a means of palliation until recently Radiation castration is fairly popular but it has the disadvantage of not completely arresting ovarian estrogen production in many cases It is curious that a well documented series of cases of surgical castration for metastatic cancer of the breast in the female has not been published Experience shows that surgical castration can produce temporary regression of this disease not infrequently in menstruants and those early in the menopause and it is usually superior to androgen therapy because of the greater chance of palliation and fewer side effects Put to a vote most women would rather have hot flashes and dizzy spells than whiskers and a male voice Therefore oophorectomy is indicated in the menstruant at the first sign of visceral or osseous metastatic disease Following failure of this procedure androgens could be tried

ADRENALECTOMY —On the hypothesis that extra ovarian estrogens are produced by the adrenal cortex and that many malignancies of the breast are estrogen dependent, bilateral total adrenalectomy after obliteration of the ovaries has been performed by several clinical groups *This has produced gratifying palliation*

in 18–25 per cent of the patients Palliation following this procedure has lasted from six months to three years Because of the extensive surgery involved and the need for careful supervision of replacement therapy the rest of the patients days, it would be gratifying if it were possible to select patients who would be sure to respond favorably Huggins feels he can predict response by the cell cytology of the primary untreated tumor, the tumor showing a high degree of differentiation being the most likely to respond Others have not been able to make such distinctions All are agreed that the slow growing tumor is more likely to show a favorable response and that in the highly anaplastic tumor failure is usual

The management of replacement therapy in adrenalectomized patients is as follows Starting 24 hours preoperatively 50 mg cortisone is given intramuscularly every six hours Just prior to surgery, 100 mg cortisone is administered orally and 1,000 ml normal saline solution is given intravenously If evidence of shock develops during surgery hydrocortisone is administered intravenously and methoxamine (Vasoxyl) is used to maintain blood pressure Five mg desoxycorticosterone may be given on the day of surgery and the first postoperative day although this is usually unnecessary Following surgery cortisone is given in doses of 50 mg every four hours for four doses every six hours for four doses and then gradually reduced to 50–75 mg per day in divided doses according to the patient s requirement Extra sodium chloride is added in doses of 3 Gm or more

daily depending on the estimated amount of electro lyte loss The administration of potassium is practically never indicated and may precipitate acute adrenal insufficiency The route of administration of cortisone and salt depends on the patient's tolerance to oral medication Care must be taken to maintain fluid balance and blood must be replaced as indicated Hydrocortisone should be added by slow intravenous drip if signs of adrenal insufficiency develop Usually the maintenance dose of 50–75 mg cortisone may be instituted by the fourth or fifth postoperative day Before discharge from the hospital the patient and her family must be briefed thoroughly as to management especially during any period of stress when the dose of cortisone must be increased manyfold temporarily The combined procedures of castration and adrenalectomy are of questionable value in patients nearing the terminal stage of the disease This procedure gives the greatest palliation if performed before irrevocable damage has occurred It is important also not to select patients who are irresponsible

HYPOPHYSECTOMY —Because of technical difficulties earlier attempts to perform total hypophysectomy for palliation of cancer of the breast resulted in permanent brain damage and incomplete removal of the organ Recently the frontal approach has greatly reduced the morbidity and improved the completeness of hypophysectomy It has been suggested that palliation following successful complete hypophysectomy is equal to castration adrenalectomy The withdrawal of certain other pituitary hormones as well as cor

ticotropins and gonadotropins, may further suppress tumor growth Replacement therapy following hypophysectomy is similar to that following adrenalectomy A temporary or permanent diabetes insipidus may require the administration of vasopressin tannate in oil (Pitressin) Hypophysectomy is still in the experimental stage and should be limited to centers where a careful evaluation of the results can be made

Cancer of the Male Breast

Surgical castration or high doses of estrogens produce tumor regression in about 60 per cent of men with metastatic cancer of the breast Adrenalectomy and hypophysectomy have both been shown to produce regressions after the tumor escapes from the effect of the previous procedures Surgical castration and the administration of estrogens in the male are discussed below

Cancer of the Prostate

Because of the frequency of cancer of the prostate in elderly men and the fact that it is seldom recognized before it has extended beyond the possibility of surgical obliteration this is the most common type of metastatic tumor seen by the family physician in the male Like cancer of the female breast this tumor metastasizes extensively especially to the bone and viscera and thereby produces many debilitating and painful lesions Months or even years may elapse before death during which the patient goes through

great suffering Fortunately however this tumor is not entirely autonomous in its growth and responds to certain steroid manipulations as does cancer in the female and male breast These procedures can provide great palliation for anywhere from three months to eight or nine years during which time the patient may be rehabilitated and can carry on a relatively normal life although at no time is the tumor so completely depressed that it disappears

CASTRATION —Removal of the testes eradicates most of the circulatory androgens In general the growth of cancer of the prostate is stimulated by androgens and inhibited by their withdrawal Castration can provide dramatic relief from crippling bone pain and pain due to tumor encroachment of sensory nerves or vital organs Urinary retention may be corrected with definite shrinking of tumor tissue Cough and dyspnea produced by invasion of the pleura and pulmonary parenchyma may be relieved dramatically These results are due to a specific effect on the metastases as demonstrated by roentgenographic and cytologic evidence A dramatic decrease of the elevated serum acid phosphatase is further evidence of the specificity of the reaction About 65 per cent of all cancers of the prostate are favorably influenced by castration Good palliation may last from three months to a number of years The results however, are temporary, since the tumor finally escapes from the effects of this androgen withdrawal Estrogens are used in conjunction with castration with apparent beneficial effects this may be due to the fact that some Leydig

cells are occasionally preserved especially when the tunica albuginea testis is left intact It would appear that if a patient accepts a procedure such as castra tion the surgeon should take every means of removing all testicular sources of androgen production

ESTROGENS—Chemical castration may be obtained by the use of estrogens in the male Five mg diethylstilbestrol (or its equivalent) daily will provide simi lar but not as prompt relief as that obtained by sur gical castration Estrogens suppress pituitary gonado tropins thus producing atrophy of the testes In some cases the combination of surgical castration and administration of estrogens seems to be of greater pal liative value than either therapy alone It is possible that the estrogens by depressing gonadotropin may suppress extra gonadal androgen formation

ADRENALECTOMY—Since the adrenal cortex secretes androgenic steroids it is not surprising that when pal liation eventually fails after suppression of gonadal sources of androgen removal of the adrenals will be of renewed aid in palliation It also appears that, when neither castration nor estrogens have been of value adrenalectomy will also fail This is probably due to the fact that some prostatic tumors are entirely auton omous Palliation following adrenalectomy in patients in relapse after either chemical (estrogen) or surgical castration is usually of short duration Because of this some clinics have dropped this form of therapy How ever adrenalectomy produced palliation has been known to last as long as 2½ years The management

of adrenalectomized patients has already been described

Hypophysectomy—Recent improvements in the technic of hypophysectomy have provided a means of depressing prostatic tumors through the suppression of both cortical and gonadal testosteroids by removing gonadotropin and corticotropin production There is some evidence that the pituitary growth hormone may also influence tumor growth therefore hypophysectomy may have the advantage of producing in a single procedure greater palliation than that provided by castration and adrenalectomy Earlier attempts to obliterate the hypophysis by radiation were unsuccessful because the amount of radiation required injured the adjacent brain tissue Recently, the hypophysis has been destroyed by the use of radioactive yttrium placed directly into the hypophysis

Adrenal corticoids—On the theory that corticoids in high doses can produce atrophy of the adrenals 200 mg cortisone (or its equivalent) daily has been used in prostatic cancer Marked pain relief especially that of bone pain can be obtained by this technic but evidence of suppression of adrenal androgens is lacking It is more likely that this palliation is due to the anti inflammatory effects of the corticoids rather than to any specific repression of the tumor

Androgens—Occasionally patients in relapse after orchidectomy will show general improvement when androgens are administered There may be improved appetite increased strength and a sense of well being However no tumor regression occurs and the sub

jective improvement is probably due entirely to the expected effect of replacement therapy in a castrate More often androgens will produce increased pain and debilitation in these patients

Use of Hormones in Other Solid Tumors

Both testosterone and estrogens have been tried in various other types of tumors with negative results although because of the anabolic action of testosterone weight gain increased strength and improved hemogram may occur Preliminary reports suggested that progesterone might be of value in cancer of the cervix but more complete studies have shown this to be without effect Estrogens may by their action on the mucous membrane of the vulva decrease the necrosis and promote some healing in far advanced cancer of the cervix but they have no inhibiting effect on the growth of the tumor The effect of cortisone and corticotropin in lymphomas and leukemias is discussed below These drugs have a valuable place in the nonspecific palliation of far advanced malignant disease in general Control of fever reduction of inflammatory reactions relief of pain improved appetite and general feeling of relief may be obtained temporarily in many patients Corticoids and corticotropin are not used often enough in far advanced malignancies probably because the action is nonspecific and does not affect the growth of the tumor itself If the patient is made to feel better this is a real contribution These drugs are of especial value in pulmonary

malignancy, whether primary or secondary, by improving the airway and decreasing edema and secretions Corticoids in large doses may produce temporary regression in cancer of the breast and have been shown to control hypercalcemia at times

Malignancies of the Reticuloendothelial System

Hodgkin's disease —The course of Hodgkin's disease can be altered by three general approaches radiation chemotherapy and steroid therapy Radiation and most of the chemical agents act by virtue of their cytotoxic properties Mitosis is inhibited or arrested and there is evidence of changes in the structure and functions of the chromosomes These effects are more pronounced on rapidly proliferating cells Although all germinal tissue is susceptible from a clinical standpoint the most important effects on normal tissue are observed in the bone marrow and lymphoid structures with less significant effects on the intestinal mucosa gonads and cornea Nitrogen mustard, TEM and TEPA are all effective in producing temporary regressions in Hodgkin's disease similar to those provided by radiation Chemotherapy may be given previous to in conjunction with or following radiation therapy depending on individual circumstances However careful hematologic studies must be made in order to prevent too great a depression of bone marrow function Radiation is generally the treatment of choice when the disease is localized and chemo

therapy is usually used first if the disease is generalized The response to chemotherapy (relief of pain pyrexia pruritis etc) may be observed in a few days If chemotherapy does not prove effective it can be abandoned temporarily in favor of radiation following which it may be reinstituted to good effect In those patients who develop anorexia generalized weakness etc corticotropin cortisone or certain other corticoids may provide valuable additive therapy Corticotropin and corticoids produce shrinking of the tumor, stimulation of the bone marrow and relief of pruritus pain and hyperpyrexia Used in conjunction with radiation or chemotherapy they frequently depress the unpleasant side effects of these procedures

LYMPHOSARCOMA.—Nitrogen mustard TEM corticotropin and cortisone have proved to be of value in the palliation of lymphosarcoma The folic acid antagonists are occasionally effective but their use should be reserved for those cases which fail to respond to other forms of therapy Radiation is an important and useful technic in the management of lymphosarcoma Corticotropin and cortisone can be used in conjunction with nitrogen mustard or TEM or alone in the same manner as described above in Hodgkin s disease with gratifying but temporary results Corticotropin and the corticoids can be particularly useful when the patient has become refractory to other forms of therapy Reticulum cell lymphosarcoma occasionally responds to treatment with nitrogen mustard or TEM Partial remissions are usually obtained in case of lymphocytic lymphosarcoma and

the best results are most often seen in cases of giant follicular lymphosarcoma using both nitrogen mustard or TEM and corticotropin or cortisone

CHRONIC MYELOCYTIC LEUKEMIA.—Myleran (1 4-dimethanesulfonoxybutane) may prove to be the drug of choice in the treatment of chronic myelocytic leukemia Radiation is usually more effective than nitrogen mustard TEM urethane and 6-mercaptopurine (Purinethol) ThioTEPA (triethylene thiophosphoramide) is being used experimentally, and colchicine (and its derivatives) has been employed in this disease although the latter drug does not significantly alter the course of the leukemic process Fowler's solution may be used advantageously in the early course of the disease however it must be noted that every accepted form of therapy shows to advantage in early myelocytic leukemia

CHRONIC LYMPHOCYTIC LEUKEMIA —This disease must not be treated on the basis of elevation of the white count only If the count is 100 000 and no anemia is present, and if no symptoms referable to the disease cause discomfort, then no therapy is indicated Since this disease is favorably influenced only temporarily by radiation chemotherapy (nitrogen mustard TEM TEPA, ThioTEPA) and corticotropin or corticoids these agents should be used only when necessary for the welfare or comfort of the patient. The rule here is "Don't treat the blood count—treat the patient."

ACUTE LEUKEMIA.—The prognosis in acute leukemia is discouraging However if we consider that it is now possible to prolong life by months or a year or

more we have reason for hope that we are on the right track and that eventually more rewarding results may be obtained If with modern therapy we can make the terminal months of a childs life comfortable and free of misery this is of no little consideration to the patient, the family and the physician Nitrogen mustard TEM Myleran and urethane are of little or no value Fortunately there are three groups of agents of proved merit corticotropin and the corticoids folic acid antagonists and 6-mercaptopurine Although resistance to these drugs always develops it is clinically important that there is no cross transfer of resistance This makes it possible for example to achieve an effective result with 6-mercaptopurine after resistance has developed to the folic acid antagonists The effects of corticotropin or corticoids are usually seen soon after institution of treatment whereas 6 mercaptopurine and the folic acid antagonists require three to four weeks before their effects are significant Accordingly corticotropin or corticoids is the treatment of choice in the acutely ill patient either at the onset of the disease or during an exacerbation while under treatment with other agents Courses of therapy with any of these three groups of agents may be given sequentially or concurrently depending upon the clinical condition of the patient It should be noted that the folic acid antagonists are usually ineffective in acute monocytic leukemia Also all of these agents appear to be more effective in children than in adults Acute leukemia in adults may respond to the combination of 6 mercaptopurine and corticotropin or corticoids The

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lymphoblastomas particularly in the early stages of the disease when the lesions are minimal in size Nitrogen mustard and TEM are generally most useful Corticotropin and corticoids will temporarily relieve pruritus and promote healing of the lesions

PHARMACOLOGIC PROPERTIES OF HORMONES AND DRUGS

Corticotropin and Corticoids

Corticotropin (ACTH adrenocorticotropic hormone) is available as aqueous and gel solutions in standard and high potency form but the most convenient form is the high potency gel because of the ease of administration and the need for only one injection a day or every two days in comparison to the necessity of giving the aqueous solution every four hours for maximum effect For more rapid effect it can be used in 10 per cent dextrose by slow intravenous drip over a 12 hour period For maximum cortical stimulation 80–100 units of corticotropin gel (40 units per cc) is given once daily for two or three days and gradually reduced to a maintenance dose of 20–40 units a day depending on the condition treated Because the drug is given daily the patient is usually instructed in the insulin technic using a U40 syringe

Corticotropin is useful in acute leukemia the lymphomas chronic lymphatic leukemia and multiple myeloma and is also of value with radio or chemo therapy in blocking some of the myeloid depressing effects and radiation sickness At times it gives good

use of very large initial doses of prednisone may prove to be the treatment of choice According to some investigators corticotropin and cortisone are contraindicated in acute myeloblastic and monocytic leukemia

MULTIPLE MYELOMA —Relief of pain has been reported following the use of stilbamidine, however since this drug is very toxic and its effectiveness in multiple myeloma is uncertain its value in this disease is doubtful Urethane is occasionally of value, but its effects are usually not seen until after four to eight weeks of treatment and only a small proportion of patients exhibit a good response Corticotropin and the corticoids provide temporary beneficial effects in about half the cases of this disease

BRONCHOGENIC CANCER

In cases in which radiation is inadvisable or must be postponed nitrogen mustard or TEM can often be used advantageously Relief of pain cough and dyspnea are frequently achieved The effectiveness of chemotherapy is usually of short duration and it must consequently be considered as a temporary although important part of the management of bronchogenic cancer Corticotropin and corticoids are of special palliative value in improving the airway and decreasing edema bronchial secretions and spasm

CANCER OF THE SKIN

Chemotherapy can often provide relief of pruritus and regression of the lesions of mycosis fungoides and

are being obtained in certain cases of acute leukemia in adults with doses of 1 Gm daily for 10 days followed by maintenance doses of 50–100 mg daily The duration of such remissions has yet to be determined Some investigators have used up to 5 Gm daily This drug in doses of 100 mg a day or less also produces great palliation in certain cases of intracranial metastases

Large doses and prolonged therapy with all of these drugs produce Cushing s syndrome with sodium retention potassium loss insomnia peptic ulcer, nervousness euphoria and occasionally mental disturbance Derangements of protein synthesis and carbohydrate metabolism depression of the thyroid amenorrhea and osseous decalcification may occur, and the physician must be alerted to these effects and reduce the dose as indicated Abrupt cessation of therapy with any of these drugs will produce acute although temporary adrenal insufficiency

ANDROGENS

The choice of androgen in the treatment of cancer depends to some extent on which route of administration is preferred The dose of methyltestosterone is 100 mg per day orally in women who have cancer of the breast Methyltestosterone has been reported to produce hepatitis and this may contraindicate its use in some cases Testosterone propionate is given intramuscularly in doses of 50–100 mg three times weekly Androgen therapy should be continued for 8–10 weeks in order to ascertain its effect Androgens will usually provide a sense of well being and may often bring

palliation in terminal states of any type of malignancy, reducing hyperpyrexia, nausea vomiting anorexia and anemia Sometimes it appears to be of greater value than the corticoids

CORTISONE ACETATE is useful in the same condition as corticotropin The initial dose of cortisone acetate is usually 200–300 mg a day, with gradual reduction to 75–100 mg for maintenance therapy Its action is more rapid but less prolonged by mouth than by the intramuscular route

HYDROCORTISONE administered in about two thirds the dose of cortisone has the same physiologic re actions as cortisone and is effective orally The anti inflammatory reaction may occur a little more rapidly This corticoid is available in alcohol solution for in travenous therapy For rapid cortical effect 100 mg of hydrocortisone in 50 cc alcohol is diluted in 500–1 000 cc of 10 per cent dextrose and given by vein over a four to six hour period The concentrated alcohol solution must never be given undiluted

PREDNISONE (Meticorten Deltasone Deltra) is effec tive in the same conditions as corticotropin, cortisone and hydrocortisone but has the advantage of having less effect on the mineral metabolism and therefore can be given in relatively higher therapeutic doses without producing as profound changes in sodium and potassium metabolism Nonspecific palliative effects can be obtained in metastatic cancer with doses of 20–50 mg daily It appears to be the steroid of choice in lymphomas frequently controlling these diseases for months with 40–100 mg daily Promising results

per cent solution of sodium citrate may be used to control a runaway hypercalcemia Corticoids are also useful in hypercalcemia, and 200 mg cortisone (or its equivalent) daily can be employed In the female estrogens usually provide a sense of well being but the physician must nevertheless be alert for those instances in which these hormones provoke an exacerbation of the malignancy The abrupt cessation of therapy will produce uterine bleeding in any female regardless of age In the male these hormones will provoke loss of libido and painful gynecomastia

Folic Acid Antagonists

The two most commonly used agents in this class are AMINOPTERIN and METHOTREXATE (also known as amethopterin) The usual oral or intramuscular dose of aminopterin is 0 25–0 5 mg and that of methotrexate, 2–5 mg The drugs are given three to six times weekly and can produce dramatic hematologic changes Daily studies of the blood and hematopoietic system are prerequisites to the proper use of these agents in the early stages of treatment Later when the hemogram is stabilized these observations may be reduced to once or twice a week The more serious reactions to these agents are leukopenia and hypoplasia of the bone marrow Lesions of the mucous membranes are an early sign of impending difficulty Bleeding in the gastrointestinal tract is usually but not always preceded by diarrhea In any event, diarrhea should be a sufficient basis for cessation of treat-

about an increase in body weight They produce a retention of sodium, and the resulting edema may provoke congestive heart failure Hypercalcemia may also occur especially in patients with osteolytic metastases The untoward effects of androgen therapy in women include hirsutism deepening of the voice acne enlargement of the clitoris and an increase in libido which may be severe enough to produce eroticism Masculinization of women may appear with doses of testosterone propionate as small as 100 mg per month The so called 'androgens of low androgenicity are of no greater value in cancer of the breast since the effective dose must be large enough to produce virilism similar to that resulting from testosterone propionate

Estrogens

Diethylstilbestrol and ethinyl estradiol have the advantages of high potency oral effectiveness and relatively low cost The usual dose of diethylstilbestrol is 15 mg daily, and that of ethinyl estradiol approximately 3 mg daily These doses are 15–30 times larger than those used for replacement therapy The common side effects of estrogens include nausea emesis and anorexia More serious are edema and hypercalcemia which may occur as the result of continuous administration of estrogens Rising calcium levels in the blood should indicate the need for prompt discontinuation of estrogens and measures should be taken to insure an adequate fluid intake As an emergency device the intravenous administration of 250–500 cc of a 2 5

MYLERAN

Myleran (1, 4 dimethanesulfonoxybutane, known experimentally as G T 41) is one of the more promising new agents in the treatment of leukemia It is effective orally and appears to be more selective in its action on myeloid cells than nitrogen mustard or the folic acid antagonists It is particularly useful in those cases of chronic myelocytic leukemia which have failed to respond to radiation therapy It has a relatively rapid onset of action and produces minimal effects on the lymphocytes and platelets except when large doses are used Careful hematologic studies should be made daily during the early stages of treatment and at least once weekly thereafter Myleran should be discontinued if there is evidence of depression of bone marrow function If there is a sudden drop in the leukocyte count during the initial treatment with Myleran the drug should be withheld until the nadir is reached Therapy can be reinstituted when the white blood cell count begins to rise Oral doses of 2–8 mg daily have been used to produce the desired decrease in the leukocytes which is usually well developed after about three weeks of treatment The duration of the remission may be as long as 12 months and repeated courses of therapy have been used to advantage The toxic effects of overdosage are thrombocytopenia and hypoplasia of the bone marrow Unlike the folic acid antagonists there is no specific antidote

ment with these agents Thrombocytopenia also may be so severe as to warrant discontinuation of therapy Alopecia sometimes occurs with long term therapy The term "folic acid antagonist" is perhaps unfortunate but it is entrenched in the literature and there would be little use in disputing it at this time That these agents do *not* act as antagonists to folic acid in man has important clinical significance The drugs act as antimetabolites by preventing or interfering with the conversion of folic acid (pteroylglutamic acid) to folinic acid (citrovorum factor) Therefore, it follows that folic acid is of no value as an antidote to the toxicity of aminopterin or methotrexate Folinic acid (citrovorum factor) on the other hand *is* an effective antidote Unfortunately, the administration of folinic acid although it counteracts the toxicity of these agents also negates their effectiveness in the treatment of leukemia

Fowler s Solution

Fowler s solution (potassium arsinite solution N F) is used in the treatment of chronic myelocytic leukemia Its use is based on the depressing effects of inorganic arsenic on the formation of white blood cells The toxic effects of Fowler s solution are accordingly the same as those of arsenic Consequently any consideration of its use must involve a comparison with the effectiveness and toxicity of other chemotherapeutic agents such as Myleran

intra arterially Nitrogen mustard is given in single doses of 0 1 mg/kg b i d for 2–3 days or once daily for 4–6 days Thus, the total dose in either schedule is 0 4–0 6 mg/kg Giving 25 mg chlorpromazine (Thorazine) orally one hour before the administration of nitrogen mustard helps to prevent nausea and emesis

URETHANE

Urethane (ethyl carbamate) is unlike nitrogen mustard and some other chemotherapeutic agents in that it does not have any special affinity for rapidly proliferating cells It resembles the other agents, however in producing the desired depression of bone marrow function Its effects are sometimes so rapidly progressive that an aplastic bone marrow (with severe leukopenia and anemia) may require immediate cessation of therapy The sedative characteristics of urethane are usually not troublesome except in ambulatory patients Nausea emesis vague gastrointestinal discomfort and hepatic damage have been reported Urethane is given orally in the form of enteric coated tablets in order to minimize the local gastric irritant properties of the drug The usual dose in leukemia is 1 Gm t i d until the leukocyte count falls to about 20 000 In multiple myeloma the dose is 1–2 Gm t i d until the desired result is achieved (usually 4–8 weeks) The low cost of urethane the ease of administration, and its effectiveness in relieving fever skeletal pain and hematologic abnormalities make it a desirable agent

Nitrogen Mustard

The cytotoxic effects of nitrogen mustard (me chlorethamine N F Mustargen) are very similar in many respects to those of radiation Therefore care ful hematologic studies should be made before giving nitrogen mustard after radiation therapy, or vice versa in order to make certain that sufficient time has elapsed for recovery of bone marrow function Within a day or two following the administration of nitrogen mustard a lymphocytopenia occurs which becomes maximal in about a week The leukopenia thrombo cytopenia and depression of bone marrow function limit the dosage of nitrogen mustard during any course of therapy Granulocytopenia and a decline in both the red blood cell count and hemoglobin are character istic consequences of therapy with nitrogen mustard Nausea emesis amenorrhea and depression of sper matogenesis are among the other common reactions Nitrogen mustard is a vesicant agent and its local toxicity is such that a special technic must be used for its administration The drug is usually given in travenously with every precaution taken to prevent its leakage into the subcutaneous tissue where it would produce sloughing A rapid flow of saline solu tion is introduced intravenously, if there is no evidence of leakage the flow is stopped temporarily while the nitrogen mustard is injected and then is again given at the previous high rate for a few minutes In some cases it is possible to focus the effect of nitrogen mustard on a specific tissue by injecting the drug

some promise of being a relatively safe and useful agent These compounds are chemically, and in some ways pharmacologically, related to nitrogen mustard and TEM ThioTEPA appears to be effective orally and can be given by intravenous or intramuscular injection without danger of venous thrombosis and with little or no nausea or emesis The limiting factors are the same as those of nitrogen mustard namely, leukopenia thrombocytopenia and depression of bone marrow function Therefore it is recommended that hematologic studies be made daily during the early stages of treatment with ThioTEPA and at least once weekly during maintenance therapy The dosage of ThioTEPA in chronic leukemia varies according to the hematologic findings and the clinical requirements Harry Shay *et al* (A M A Arch Int Med 92 628, 1953) used 2 5 or 10 mg intramuscularly The total dose varied from as little as 28 mg to more than 500 mg In chronic leukemia ThioTEPA is given as needed until the desired hematologic response occurs the minimal effective maintenance dose is used thereafter It is recommended that the patient receive a high fluid intake There have been conflicting reports of the usefulness of ThioTEPA in solid tumors

6 Mercaptopurine

This drug (Purinethol) acts as an antagonist to hypoxanthine and adenine and is thus an antipurine It differs from the folic acid antagonists both by its mechanism of action and by the fact that there is no

Triethylene Amine (TEM)

TEM is considered to have the same type of cytotoxic action as that of nitrogen mustard It has significant advantages however, in that TEM is effective orally and produces less nausea and emesis than does nitrogen mustard The absorption of TEM from the gastrointestinal tract is somewhat erratic however absorption can be facilitated by the simultaneous administration of sodium bicarbonate Oral dosage schedules range from 5 mg daily for from 2 to as many as 10 successive days Two grams of sodium bicarbonate are usually given orally with each 5 mg dose of TEM It is important to note that the maximal effect of TEM usually occurs about 10 days after initiation of therapy therefore time should be allowed for these effects on the bone marrow to be assessed before starting a new course of therapy or continuing the administration of TEM This delay in the onset of action makes TEM less desirable than nitrogen mustard in cases where a rapid effect is needed The systemic toxicity of TEM and the precautions attending its use are in general the same as those of nitrogen mustard

Ethylene Phosphoramide Derivatives

Three of the ethylene phosphoramide derivatives which have been studied clinically are DEPA (diethylene phosphoramide) TEPA (triethylene phosphoramide) and ThioTEPA (triethylene thiophosphoramide) Of these three ThioTEPA seems to have

A Cancer Res 2 11 1955) reported on the use of OPSPA in more than 100 patients with solid tumors who were observed for periods of 1–18 months The drug was given either intramuscularly, into serous cavities or directly into the tumor There was some evidence of temporary palliation which should en courage further investigation of the use of this agent Like the other ethylene phosphoramide derivatives OPSPA can produce a severe leukopenia

Studies in animals are being carried out with many other chemical compounds some of which are under going clinical trial Among these are agents such as azaserine demecolcin 6-thioguanine azaguanine and desoxypyridoxine

known antidote to 6-mercaptopurine It is important that complete hematologic studies be made daily during the initial stages of therapy and at least once weekly thereafter Since the maximal effect on the hematopoietic system may be delayed for several days the drug should be discontinued temporarily at the first sign of a precipitous fall in the white blood cell count Toxicity arising from overdosage includes hemorrhage leukopenia anemia and thrombocytopenia Dosage of 6 mercaptopurine must be adjusted on the basis of the hematologic and clinical findings Usually, 2 5 mg/kg per day orally is the initial dose If after one month of treatment there is no evidence of depression of the leukocytes and no clinical improvement the dose is increased up to 5 mg/kg daily If the leukocyte count falls the drug should be discontinued and after the count has remained constant for several days or begins to rise a suitable maintenance dose should be initiated It should be remembered that unlike some other chemotherapeutic agents 6-mercaptopurine *must* be given in maintenance dosage if an early relapse is to be prevented It is best to seek the minimal effect dose of this drug at all times and especially in those patients with impaired renal function

Experimental and Miscellaneous Agents

OPSPA (oxapentamethylenediethylene thiophosphoramide) is a recent addition to the ethylene phosphoramide derivatives A R Curreri *et al* (Proc Am

surgeon who is capable of relieving the patient's pain by an operative procedure The two procedures obviously go hand in hand and represent a form of medical teamwork

The general surgical procedures discussed here are those that are used primarily in dealing with patients afflicted by a malignant disease that has reached an advanced stage The operations mentioned do not in any sense constitute definitive therapy of any specific cancer The discussion is confined to certain procedures which may extend life and alleviate pain and discomfort of incurable neoplastic disease

GENERAL CONSIDERATIONS

Before attempting to analyze special situations calling for surgical intervention in the care of patients with advanced cancer certain basic considerations should be reviewed They are common to practically all patients with this form of illness and they form the background in which the surgeon develops the tactical approach which he must apply to the treatment of his patient

TYPE OF NEOPLASM —Cancer must usually be considered in the category of chronic rather than acute illness This is true even of the far advanced cancer no longer amenable to definitive therapy as well as of the early neoplasm The degree of chronicity, however depends on many factors The most important is the histological type and biological characteristics of the specific neoplasm This can best be illustrated

CHAPTER 5

Surgical Procedures in Control of Pain in Advanced Cancer

AN OLDER PHYSICIAN used to admonish his residents Cure some help many comfort all At no other time in the practice of medicine can the physician apply this advice more aptly than when he is treating a patient suffering from cancer that is incurable from its outset or for which treatment has failed

Before embarking upon a discussion of specific procedures that may be applied to situations created by malignant disease it is necessary to realize that the surgeon is but one member of a medical team available to treat the pain and distress of patients with advanced cancer Any efforts on the part of the surgeon to help his patient must be carried out within the framework of the capabilities of the entire medical team For example it would seem ill advised indeed to prolong the life of a patient who is suffering from advanced cancer of the cervix limited to the pelvis by diverting the urinary stream if one failed to take into consideration one member of the team a neuro

Extent of lesion —The estimation of the local anatomic extent of a neoplasm and of the presence or absence of metastases, even though not absolute, gives some insight into the patient s prospect for continued survival Cancer may destroy its host in many different ways Local extension of the primary lesion regardless of its metastases may destroy some organ or function that is vital to the patient s bodily economy By metastases, a cancer may reach the same end point and there are other ways in which the parasitic growth overwhelms the bodily economy of the host on a quantitative basis Obviously, then the greatest palliation and extension of life may be expected in instances in which the tumor is destroying its host through its local effect Advanced tumor limited to the pelvis is an excellent example of such a situation Many patients die of advanced cancer of the uterus or prostate without evidence of extension of the neoplasm outside the anatomic confines of the pelvis Death from cancer limited to the pelvis not infrequently occurs in rectal and bladder cancer although this is not as common as in prostatic and uterine cancer In all these instances obstruction of the urinary excretory system at the lower third of the ureters contributes heavily to the mortality rate Since all of these lesions tend to produce obstructive hydronephrosis with pyelonephritis, kidney failure with uremia is a fairly common cause of death Pain is similarly a common problem in that by local extension the sciatic plexus of nerves very shortly becomes involved in tumor There are surgical methods to correct

by means of the survival curves of patients who have various types of cancer but are treatable Failure of specific therapy in curable cases gives us a fair picture of some of the characteristics of various cancers In some cases failure is prompt as is death from failure in others failure occurs and is sustained over a long period of time It is known, for example that patients with incurable breast cancer usually die within the first two years after the diagnosis was made However a surprising number of patients whose breast cancer has been deemed incurable continue to survive even longer than five years—the yardstick familiar to all who treat cancer On the other hand most melanocarcinomas when inoperable are fatal within 12 months This disease then is apparently less chronic in its evolution than is breast cancer Again there are patients who have survived amazing lengths of time with known incurable melanocarcinoma As a larger number of tumors are studied in this manner it becomes fairly evident that each specific histological type of lesion has a natural history of its own determined primarily by its biological characteristics Each has predilections as to the anatomic sites at which the primary tumor arises Each specific tumor has some characteristic manner in which it metastasizes as well as a manner in which it produces local destruction Unfortunately at this time we are unable to predict accurately the biological growth characteristics of any given tumor furthermore we are unable to select the individual who is destined to survive any appreciable length of time whether treated or not

damage complicate the patient s problem the surgeon might in the face of incurable disease be justified in choosing the simpler operative procedure This type of reasoning would not, however apply to a patient with clinically curable rectal cancer even though his problem was complicated in the manner just described The final decision in balancing the general physical status of the patient with the proposed operation must rest primarily on the surgeon and be governed by his experience Since there is no exact guide to such de cisions the evaluation of risk in a patient can usually be summed up in the simple statement "What is best for the patient is best for the doctor"

Attitude of patient —The attitude of the patient to any situation created by the disease varies tremend ously it is given direction and impetus by numerous factors many of which are immeasurable They are more thoroughly evaluated in Chapter VII Attitude is mentioned here only as it relates to the employment of surgical therapy In the long run the final answer to any surgical problem is the patient s clear under standing of the situation and his acceptance or rejec tion of the surgical plan of treatment

The preceding paragraphs outline in the general way the key factors which a surgeon must consider in deciding on a course of treatment for his patient The procedure must offer some degree of alleviation of the patient s symptoms either as a result of the operation itself or in conjunction with some other form of therapy The relief of pain of course is of paramount importance However the relief of any form of dis

both of these difficulties and achieve extension of life and relief of pain in a fair number of these patients

TYPE OF DISABILITY —Death from any specific type of cancer is indeed protean It usually occurs when some vital function or functions are destroyed Even though a tumor is far advanced and incapable of cure it is often possible for the surgeon to restore or substitute for some vital function that is becoming lost to the disease and to postpone death at least temporarily Intestinal obstruction that results from the invasion of the bowel by a neoplasm is an excellent example in this case, simple surgery gives much relief

GENERAL PHYSICAL STATUS OF PATIENTS —It has often been said that there are few if any medical contraindications to the treatment of cancer This statement applies primarily to those lesions which are amenable to definitive attack and provide the patient with the hope of a reasonable chance for survival However this attitude is not generally applicable to the individual in whom a malignant neoplasm has developed to the point where death is inevitable In such a case the physician must make a serious effort to evaluate the possible rewards of a surgical procedure against the poor outcome of treatment which might result from the presence of some secondary complicating organic illness Not infrequently this problem arises in connection with rectal cancer *Even in the presence* of hepatic metastases patients live on the whole as long and most assuredly more comfortably after an abdominal perineal resection of the rectum than after a *simple colostomy But should extensive cardiac*

chest tend to produce respiratory obstruction (1) tumors that are primary within the tracheobronchial tree (primary bronchogenic cancer), (2) far advanced cancer occurring within the lower portion of the upper third or the middle third of the esophagus and (3) tumors arising primarily in the mediastinal lymph nodes (as, for example, lymphomas) or as the result of metastatic cancer in the mediastinal nodes particularly in the region of the pulmonary hilus Respiratory obstruction has occurred as the result of metastatic disease in the mediastinal lymph nodes secondary to primary lung, esophageal and breast cancer, to cite but a few examples When respiratory obstruction results from cancer within the thorax, the surgeon is at a loss to supply the patient with any adequate airway Although there are reports that airways have been provided surgically through the thoracic wall, these operations have usually been done after trauma to the thorax with injury to the tracheobronchial tree rather than in an effort to relieve the obstruction produced by a malignant neoplasm within the chest Most respiratory obstruction at this level that is caused by cancer results not so much from extrinsic pressure on the tracheobronchial tree as from direct invasion of this structure Hence the decompression operations (sternotomy) that have been carried out with some degree of success in rapidly expansile lesions within the chest (that is, aortic aneurysm) are not applicable to the treatment of invasive cancer Little or nothing can be accomplished by surgical technics to relieve the respiratory obstruction within the chest that is

comfort—for example asphyxia hunger thirst intestinal cramping nausea or vomiting—is about on a par with relief of pain The ability of an operative procedure to extend life so long as that life remains comfortable is also to be desired, but no physician is required on moral grounds to extend the life of a patient which when extended, would only make the patient more miserable The only situation that demands this heroic form of treatment must arise at the specific request of the patient. The operative risk of any contemplated surgical procedure must be estimated, and this estimate must be presented to the patient when the proposed procedure is discussed in order that he may apply it to his scale of values in either accepting or rejecting the advice of his surgeon

SPECIFIC SITUATIONS REQUIRING SURGICAL INTERVENTION

Respiratory Tract

Obstructions of the respiratory tract that result from invasive cancer are conveniently divided into two main groups The first consists of obstructions that arise within the thorax below the suprasternal notch The second group consists primarily of tumors that involve the respiratory tree above this point This division is actually not quite this arbitrary since the surgeon is usually unable to relieve respiratory obstruction within the thorax but can restore an adequate airway when obstruction occurs within the larynx or above it.

Three major groups of tumors occuring within the

out this procedure as an elective operation Urgent tracheotomies are best done under local anesthesia however as a lifesaving procedure when time is an important factor anesthesia is not necessary The hypoxia produced by the respiratory obstruction in such emergencies tends to dull the patient and acts as an anesthetic by itself

Every physician should be capable of carrying out a tracheotomy when the occasion arises, for the procedure is simple After proper preparation and local infiltration of 10 per cent procaine (time for this should not be wasted in urgent situations) a simple longitudinal incision is made in the midline of the neck and carried down through the ribbon muscles above the isthmus of the thyroid The lower border of the cricoid cartilage and the first three tracheal rings are exposed by the division of the pretracheal fascia The second or third tracheal ring is grasped by a fine sharp hook and a linear incision is made to divide the second and third tracheal ring opening the airway A small block of cartilage is excised from each of these rings to assure a patent airway A tracheotomy tube with its obturator is then inserted into the trachea and the obturator removed The tube is tied in place around the neck and the incision is closed by interrupted black silk sutures in anatomic layers to close the skin around the tracheotomy tube This airway is kept clean by means of intermittent suction whenever necessary In extremely urgent situations it may be necessary as a preliminary measure to insert a large no 13 gauge needle into the trachea or to thrust

caused by primary or metastatic cancer Such relief remains a problem for the radiotherapist

Above the level of the suprasternal notch the encroachment of a cancer upon a patient's airway becomes another problem but by and large obstructions in this area can be handled in a satisfactory manner Obstruction usually occurs as it does within the thorax, by direct invasion of the tumor and this invasion gradually obliterates the airway by the very bulk of the tumor rather than by pressure effects Most frequently obstruction is caused by a primary epidermoid cancer arising within the larynx but far advanced lesions of the base of the tongue and of the hypopharynx may also obliterate the airway Cancers within the oral cavity or nasopharynx seldom produce an obstruction of such severity that the patient's airway is in actual danger Occasionally primary cancers arising in the thyroid or parathyroid may invade the trachea and cause respiratory obstruction however, this is not the usual course of these neoplasms Only rarely do cervical lymph nodes that have become involved, either in primary tumors of lymph node origin or in matastatic cancers enlarge sufficiently and invade the larynx or trachea to produce obstruction

It is quite feasible to short circuit the respiratory passages by means of a tracheotomy Occasionally this procedure must be carried out as an emergency when respiratory embarassment jeopardizes the patient's life In ordinary circumstances however the gradual development of stridor and progressive dyspnea provide an adequate warning *It then becomes possible to carry*

swallow his own secretions represents the lesser of the two evils Ideally, the ultimate in palliation is achieved by resection of the offending lesion However, when this cannot be accomplished because of a nonresectable lesion resort must be made to some other device Oftentimes even though the hypopharyngeal and esophageal cancers are inoperable and incapable of cure radiation therapy will make it possible for the patient to swallow and do much to relieve the pain and discomfort at least temporarily

Within the oral cavity, lesions involving the floor of the mouth, gingiva buccal mucous membrane and tongue can, if uncontrolled severely upset a patient s nutrition and fluid balance In this situation, there is no actual mechanical obstruction but invasion of the oral and pharyngeal musculature make mastication and swallowing mechanically difficult and extremely painful, and this is a terrific deterrent to an adequate intake of food and water

Lesions arising in the oropharynx can usually be circumvented by the simple insertion of a plastic nasal feeding tube Recent improvements in the types of feeding tubes available and of tube feedings make it possible to sustain a patient comfortably for weeks and even months if necessary Extension of the patient s life in this manner will provide the time needed for other members of the medical team to achieve relief of pain In lesions which obstruct the digestive tract at the hypopharynx or below it is usually not possible to pass such a feeding tube and consequently some sort of operative procedure must be car

a trocar into the trachea to provide adequate ventilation while equipment is being secured to carry out the tracheotomy

Upper Digestive System

Lesions producing obstruction in the upper digestive system occur most frequently from the level of the hypopharynx to the pylorus of the stomach In the hypopharynx and esophagus these cancers are usually epidermoid in character They may occur anywhere within the anatomic region but are seen most frequently in the lower third of the esophagus next in order of frequency at the level of the hypopharynx then in the upper third and finally in the middle third In the stomach adenocarcinoma located either at the cardioesophageal junction or at the pyloric outlet are the primary offenders so far as the production of obstruction is concerned

The most miserable symptoms of an obstruction of the upper digestive system are dysphagia, regurgitation nausea and vomiting sticking pain within the chest and aspiration of gastrointestinal contents into the tracheobronchial tree as a result of vomiting or regurgitation People who are unable to swallow either food or liquids perish very shortly unless a substitute is provided to circumvent the inability to maintain their nutrition and fluid and electrolyte balance Trouble also arises from the inability of these individuals to swallow their own secretions from the respiratory tract and the salivary glands However if nutrition can be maintained the patient's inability to

tumor infiltrating the stomach wall This operation makes it possible for the patient to resume eating and drinking in a normal manner However, in instances of stomach cancer in which the obstruction is at the region of the pylorus and the stomach is diffusely in filtrated by cancer it is impossible to perform a gastro jejunostomy It is then necessary to utilize the small bowel as the site into which fluids and feedings are administered In the extremely poor risk patient, a simple Witzel type of jejunostomy may be performed The jejunostomy should be done as close to the liga ment of Treitz as is technically feasible in order to utilize the largest possible absorbing surface of the small bowel In the better risk patient the divided Roux Y type of jejunostomy may be carried out with anastomosis of the upper portion of the divided bowel in an end to side fashion with the jejunum below The portion of the Y to be carried out as a jejunostomy must exceed eight inches in length Segments of bowel shorter than this facilitate the regurgitation of bowel contents through the ileostomy stoma and such re gurgitation causes marked skin excoriation which can become quite troublesome If the feeding loop is long enough regurgitation is never much of a problem Some caution must be used in both the speed of ad ministering the tube feedings and their concentration when introduced into the small bowel Concentrated feedings cannot be tolerated initially and are usually followed by diarrhea and cramping In some instances when administered fairly rapidly these feedings pro duce symptoms similar to the dumping syndrome that

ried out to alleviate the patient's inability to swallow

Lesions producing obstruction at the level of the cardioesophageal junction or above can be circumvented by means of a simple gastrostomy Many types of gastrostomies are described in the standard operative texts However the simplest type, a Stamm gastrostomy can be carried out with very little operative trauma The operation may be readily completed utilizing intercostal block and infiltration type of anesthesia and will provide for many months a stoma adequate for the nutrition of the patient The procedure is usually carried out through a left rectus muscle-splitting incision placed high in the left upper quadrant A stab wound is made in the anterior wall of the stomach through which is passed a large Pezzer catheter Three concentric purse string sutures are placed about the catheter and tied The anterior wall of the stomach is anchored to the parietal peritoneum by means of interrupted sutures The abdominal incision is closed in anatomic layers about the catheter *A sterile dressing is applied and usually within 12–24* hours fluids may be given through the new opening This type of gastrostomy functions as well in most cases as the more complicated varieties

In cancer of the pylorus of the stomach which is still limited to the area but locally nonresectable to maintain the continuity of the gastrointestinal tract it is best to by pass the tumor by means of a gastroenterostomy The location of this short circuiting operation depends largely on the region of the stomach which is most dependent and yet well away from

(when metastases have occurred either to liver or to peritoneum, or the primary tumor has directly involved other viscera or the abdominal wall), the lesion still develops slowly and much can be done to prolong a patient's life and make existence more comfortable. With knowledge of the behavior of this type of cancer it then seems best to resect the primary lesion, whenever possible. This should be done not only because these lesions produce intestinal obstruction but also because they are a constant source of chronic blood loss and infection, complications which take their toll by gradually sapping the patient's general physical condition and sense of well being. If because of the extent of the primary lesion it is not possible to excise it, the gastrointestinal tract must then be diverted.

In the case of obstruction of the distal half of the large bowel (left colon and rectum), a colostomy is required. Because of the fluid conserving function of the colon, when a diversion of the large bowel is necessary, as much unaffected bowel must be spared as possible in an effort to produce a colostomy that can be adequately controlled. The so called "wet" colostomy leaves much to be desired both from the physician's and the patient's point of view. Where colostomies are used to divert the fecal stream as a permanent measure, the completely divided type of colostomy is by all odds preferable to the simple loop type. The former eliminates the possibility of spillover of fecal material into the distal loop and more effectively defunctionalizes the bowel distal to the colostomy site.

follows subtotal gastric resection However, if nutritive solutions are started slowly, these complications can usually be avoided or at least minimized

Lower Digestive System

Dysfunction of the lower digestive tract produced by advanced cancer implies intestinal obstruction, although occasionally the development of an intra abdominal abscess with the formation of fecal fistulas heralds the presence of far advanced bowel cancer Simple mechanical intestinal obstruction is encountered more frequently, however than any other single complication in tumors arising in this anatomic location and an obstruction from advanced cancer in the lower digestive tract usually implies a cancer of the large bowel Although primary tumors of the small bowel are infrequent small bowel obstructions sometimes occur in the late phase of large bowel cancer or cancer of other intra abdominal viscera and usually result either from the direct invasion of the small bowel by such a lesion or from the progression of peritoneal implants

No matter what the cause of intestinal obstruction there are certain principles which the general surgeon must keep in mind when dealing with this problem Large bowel cancer is noted primarily for its slow local development and slow progression from onset to termination Indeed in many instances, months elapse before there is any evidence of metastases from such a cancer Even in the late phase of a patient s illness

may occur either as a manifestation of a primary tumor or secondarily from involvement of the small bowel by cancer arising at another site Again, whenever feasible, maximum palliation may be obtained from the resection of the lesion that has produced the obstruction When this is not possible a short circuiting operation should be carried out to restore the continuity of the intestinal tract This can be done either by totally defunctionalizing the small bowel involved or, more simply by making a side to side enteroenterostomy In this situation the anastomosis acts very much like a penny put in a fuse permitting overflow into the unaffected small bowel below the site of obstruction Rather large segments of small bowel may be defunctionalized without any permanent effect on a patient's nutritional status Because of the shortened small bowel diarrhea may occasionally result, but usually it is only temporary and can be controlled by medical and dietary management

Liver

There is no worthwhile palliation to be gained from the surgical treatment of primary liver cancer or metastatic cancer involving the liver parenchyma The only exception is in the treatment of solitary hepatic metastases or solitary primary lesions of the liver which are found to be technically resectable

Extrahepatic biliary obstruction can be relieved surgically Of the tumors that produce obstructive jaundice cancer of the head of the pancreas is the most frequent with primary carcinoma of the extrahepatic

When obstruction occurs in the ascending colon or cecum and if the lesion is nonresectable it becomes necessary to by pass this area by means of a sidetracking operation This is most usually accomplished with an ileotransverse colostomy As in the case of the distal colon, it is better so far as the patient is concerned to divide the bowel proximal to the lesion to make a complete diversion of the gastrointestinal tract This is usually carried out as an end to side ileotransverse colostomy and the distal segment of the terminal ileum is brought out to the abdominal wall to form a mucous fistula This complete diversion of the fecal stream from the region of the tumor tends to reduce infection and recurring blood loss A cecostomy should be reserved only for the decompression of an obstructive lesion in the ascending or transverse colon which can be treated in a definitive manner at a second operation A cecostomy is ineffective as far as the complete and permanent defunctionalization of the bowel is concerned and if used for this purpose proves unsatisfactory The cecostomy will work only so long as the obstruction is complete and the bowel proximal to the obstruction is filled with fecal material The patient will usually continue to have some degree of symptoms in addition to the trouble of controlling the liquid fecal material that extrudes from the cecostomy When it is not feasible to divide the small bowel completely a certain degree of defunctionalization may be obtained from a wide side to side ileotransverse colostomy

As previously pointed out small bowel obstructions

the patient s fluids and electrolytes and this loss must be compensated by the ingestion of either the bile that is lost or animal bile substitutes From the standpoint of operative safety, however, cholecystostomy represents the least traumatic of all the decompres sion operations Biliary shunts can be made from the gallbladder to the stomach to the duodenum or to a loop of jejunum In most instances though it is not desirable to use the gallbladder to drain obstructive jaundice caused by cancer particularly if the short circuit is to be permanent, for as time goes on, the neoplasm that produced the initial obstruction sometimes extends to involve the cystic duct obliterating the shunt Jaundice then recurs

When a lesion is located in the head of the pancreas it is more desirable to divide the common duct and reanastomose the proximal end into one of the nearby hollow viscera The most satisfactory approach is the anastomosis of the common bile duct into a defunc tionalized loop or limb of jejunum Again, as in the feeding jejunostomy this limb should be long enough to prevent the regurgitation of gastrointestinal con tents since regurgitation, if it occurs tends to cause repeated episodes of ascending cholangitis This con dition can be eliminated by making certain that the limb used to drain the common duct is adequate in length These anastomoses are usually carried out in two layers using interrupted black silk sutures throughout The reanastomosis of the proximal end of the common duct into the duodenum although quite effective in relieving the obstruction occasion

biliary tree, the gallbladder and the ampulla of Vater following in order of frequency Other cancers arising in this immediate anatomic area have also been noted to produce this distressing symptom, these include stomach cancer, primary duodenal cancer and in one particular case lymphosarcoma arising in the lymph nodes of the porta hepatis and occluding the common bile duct

With the possible exception of cancer of the ampulla of Vater definitive types of operative procedures, such as pancreaticoduodenectomy produce little other than palliation when the effects of treatment are measured in terms of survival Nevertheless whenever it is possible a lesion still confined to the head of the pancreas should be treated as curable cancer and resected In the vast majority of cases the major benefit derived from this radical form of surgical treatment is the relief of the symptoms of obstructive jaundice The symptoms of pruritus digestive disturbances blood clotting derangements bleeding tendencies associated with jaundice and, finally hepatic failure itself, call for prompt and energetic surgical efforts to relieve the obstruction This is necessary for the welfare of the patient, even though cure is impossible

There are many ways in which such decompression of the obstructed extrahepatic biliary tree can be accomplished The simplest of course is drainage of the biliary system by simple cholecystostomy if the cystic duct is in direct continuity with the obstructed portion of the common bile duct But this is the least satisfactory because it produces a constant drain on

creas the obstruction may once again be relieved by simply opening the clamp on the vertical limb of the T tube This procedure has been carried out on several patients who survived for surprising lengths of time without further jaundice and were quite comfortable during their terminal illness

Obstructive jaundice should be relieved surgically whenever possible However unless the jaundiced pa tient is properly prepared for surgery of this type (see any standard text relating to surgical care) the mortal ity rate of such operative procedures is quite high The operative mortality is also directly proportional to the length of time that the patient has been jaundiced

Urinary Tract

Advanced cancer arising in the kidney does not usually produce symptoms or functional derangements that are readily alleviated by surgery In certain in stances in which pain and/or secondary infection oc curs it is desirable if at all possible to remove the offending kidney This can be done for the relief of symptoms even if it is necessary to cut through the tumor In a kidney lesion accompanied by ulceration into the kidney pelvis chronic blood loss through the urinary excretory system may be difficult to manage by means of simple blood replacement If such a kid ney can be surgically removed the necessity for repeated blood transfusions may be eliminated

Cancer of the urinary bladder as it becomes ad vanced frequently requires some form of surgical in

ally fails before the death of the patient owing to the local extension of the primary tumor

When the common bile duct is the site of the primary cancer the distended obstructed hepatic radical above the primary lesion may occasionally be used to drain the liver In this situation the open end of the jejunal limb is simply sutured into the hilus of the liver If the hilus is invaded it is often impossible to locate the hepatic radicals When this occurs the left lobe of the liver may be subtotally resected thus opening across dilated portions of the intrahepatic biliary ducts The ducts are then anastomosed to defunctionalized limbs of small bowel in much the same manner as the tail of the pancreas is anastomosed to the bowel when a subtotal pancreaticoduodenectomy is carried out This however is a heroic procedure, usually too extensive for the far advanced cancer patient it is commonly reserved for the patient whose extrahepatic biliary tree has been destroyed by previous surgical trauma

One other point should be brought up Occasionally it has been possible to relieve obstructive jaundice by simply performing a choledochostomy and literally forcing a T tube along what would be considered the normal tract of the common duct through the tumor in the head of the pancreas into the duodenum The T tube is sutured in place and after a few days the external limb of the tube is clamped allowing bile to drain along the horizontal portion of the tube into the duodenum Should further extension of tumor occlude the portion of tube that traverses the pan

SO 1511, 1950), is by far the most satisfactory form of urinary diversion The anastomoses made in this operation consist of end to side ureteral ileostomies carried out by means of very fine interrupted sutures The mucosa of the ureter is sutured directly to the mucosa of the bowel to provide complete apposition This anastomosis is usually stabilized by a second layer of three or four interrupted very fine black silk sutures in order to take tension off of the anastomosis This type of ureteral anastomosis produces far fewer complications in the form of ureteral strictures and secondary obstructive hydronephrosis With the use of these ileal segments recurring episodes of pyelonephritis are fewer and the patients have far less trouble The anastomosis of the ureters into the intact bowel, usually at the level of the rectosigmoid is attended by a much higher incidence of pyelonephritis However when life expectancy is limited not by the anticipated ascending renal infection but rather by the cancer itself the anastomosis of the ureters into the intact bowel is certainly justified

After the diversion of the urinary stream has been carried out it is possible to achieve further extensive palliation by radiotherapy When radiation therapy is to be used with a view not only of relieving symptoms but actually of extending life it is desirable to use the ileal segment as a reservoir in the diversion of the urinary stream for the reasons mentioned above From the standpoint of the patient s comfort, the ileal bladder represents the ideal in bladder substitution The urine which flows continuously from the ileostomy

tervention to provide palliation The major symptoms are hemorrhage with retained bladder clots, and, superimposed on this ulcerative bleeding lesion, a secondary cystitis usually develops This combination of bleeding and infection causes symptoms that are extremely difficult to control the most prominent of these are hematuria, dysuria pyuria urgency frequency and tenesmus When the cancer is situated in and about the trigone of the bladder, the symptoms become exaggerated and much more difficult for the patient to tolerate In addition, obstruction of one or both ureters occurs in lesions situated in the bladder trigone and superimposes hydronephrosis and pyelonephritis on an already uncomfortable patient The symptoms of locally advanced bladder cancer certainly demand surgical attention

Much relief can be obtained by the surgical diversion of the urinary stream which can be accomplished in any one of several ways In order of simplicity so far as surgical technic is concerned the procedures are (1) the cutaneous ureterostomies (2) the implantation of the ureters into the large bowel usually the sigmoid colon (3) the diversion of the large bowel by means of a colostomy utilizing the rectosigmoid and rectum as a separate urinary pouch into which the ureters are anastomosed and (4) the construction of an isolated loop of small bowel brought out of the abdomen as an ileostomy into which the ureters are implanted From the standpoint of ease of care and comfort to the patient the so called ileal bladder as described by Bricker (S Clin North America

that radiates into the hips and down the lower extremities in the distribution of the sciatic nerves When the iliac lymph nodes and iliac veins become the site of metastatic cancer, progressive marked lymphedema of one or both extremities is also noted Any or all of these symptoms of advanced cancer demand relief if possible

The need for relief of these symptoms was recognized long ago and from this need have developed many courageous attempts to achieve palliation These efforts were spearheaded by Brunschwig who has pioneered a large field of salvage surgery in the treatment of cancer and who is credited with the development of the operation known as pelvic exenteration We have been using this operation or a variant for five years in the treatment of postradiation persistent cancer of the cervix Although this procedure may be classified as salvage surgery it should be carried out only in those patients who, on exploration are found to have cancer which is definitely limited to the pelvis and which can be encompassed surgically by the removal of the entire pelvic contents However an operation so extensive that it produces an operative mortality rate of approximately 20 per cent and results in the mutilation of a patient does not seem to be justified unless the patient stands a reasonable chance of remaining free of the disease following the surgical procedure

When it becomes necessary to transect a tumor in order to carry out a pelvic exenteration it is far better palliation to leave the pelvic organs in place and

stoma, may be collected in a bag sealed to the skin by an adhesive that eliminates the patient's chances of wetting his clothing with urine This bag and the ileostomy stoma are readily cared for by the patient after very little instruction

Female Genital System

Of all of the variants of female genital cancer probably the most important, from the standpoint of incidence is carcinoma of the cervix uteri Failure of control following the primary treatment of this particular cancer produces the equivalent of advanced cancer in the female pelvis Autopsy studies on this particular cancer have indicated that the large percentage (approximately 40 per cent) of the patients die of the disease without evidence of extension beyond the pelvis When the disease extends locally the sequence of events is fairly predictable In the immediate area of the cervix persistence and extension of cervical cancer often produces rectovaginal and/or vesicovaginal fistulas Extension from this point or failure of control of the lesion in the parametrium soon results in involvement of the distal segments of the ureters These gradually become obstructed by tumor and slowly progressing hydronephrosis with pyelonephritis develops terminating in death from uremia In addition, failure to control cancer of the cervix out along the pelvic walls shortly results in involvement of the nerves of the sciatic plexus The invasion of the sciatic plexus produces intense pain

advanced ovarian cancer the large primary lesion has been resected surgically, followed by radiotherapeutic efforts to control the abdominal metastases and the patients have survived for considerable lengths of time without the necessity of frequent paracentesis to relieve their symptoms

Patients who have advanced carcinoma of the vulva frequently experience considerable relief of symptoms even when the disease is incurable provided the local lesion is adequately removed The pain pruritus and burning in the region of the vulva are extremely dis tressing If these symptoms can be eliminated, the patient is much more comfortable during her terminal illness The advanced groin metastases are discussed later in this chapter

Male Genital System

The surgical removal of testicular tumors is an in tegral part of the diagnosis and primary treatment of testicular cancer Hence in the terminal phases the primary tumor is of little or no consequence It is usually the distant metastases of this particular can cer as they involve other organ systems that may require surgical intervention The site from which the primary tumor was removed rarely creates a problem in management

Palliation of prostatic cancer which is not resect able locally is primarily achieved by alteration of the patient s hormone balance The rationale of this form of treatment and that of more extensive procedures such as adrenalectomy are discussed in Chapter IV

simply divert the urinary and/or fecal stream As in bladder cancer, the isolated ileal bladder in which the ureters are anastomosed provides the most satisfactory urinary diversion This is true particularly when it is necessary to perform a sigmoid colostomy to divert the fecal stream in the same patient There is little if anything to recommend the so called 'wet colostomy Since uremia is the usual cause of death in these patients diversion of the urinary stream actually tends to prolong the patient s life With the prolongation of life after the urinary and gastrointestinal tracts have been diverted for palliative purposes it is obvious that next in the sequence of events, as far as the patient is concerned, is invasion of the sciatic plexus by the persistent cancer This complication then becomes a pure problem of alleviation of pain which can be readily and satisfactorily controlled by a neurosurgical operative procedure or by some of the technics available to the anesthesiologist

When carcinoma of the endometrium becomes too extensive or treatment fails it resembles cancer of the cervix in many ways The approach to the problem of persistent carcinoma of the endometrium is in all respects similar to that outlined for cancer of the cervix

The primary symptoms of advanced carcinoma of the ovary are those referable to abdominal ascites and to the ever enlarging primary intra abdominal mass Usually surgery offers little, if any palliation of these advanced lesions This disease is primarily a problem for the radiotherapist *However, in some instances of*

activity Surgical amputation of the penis is more or less mandatory for the control of these symptoms even though the lesion may have extended, by metastases, to the point where it is no longer curable

Large, Ulcerated, Bleeding Tumor

There is a large heterogeneous group of tumors which even though they may advance beyond the point of definitive treatment because of distant metastases can still be treated with the primary object of relieving pain or other symptoms These tumors produce many and varied types of symptoms, all of which are annoying to the patient The symptoms are usually related to (1) the size of the lesion (2) the anatomic location of the lesion (3) ulceration of the skin in the region of the primary tumor, (4) bleeding from the ulcerated site and (5) infection and necrosis in an ulcerated tumor Even though the disease has progressed beyond the bounds of possible cure, these lesions should be excised whenever possible to alleviate the local symptoms and to simplify nursing care This is particularly true when the cancer not only has become large and ulcerated but also has destroyed the function of the area involved In the treatment of cancer one encounters many situations of this type but specific reference will be made to only a few

Inoperable cancer of the breast —Evaluation of the inoperability of any given breast cancer is best based on Haagensen and Stout s criteria However,

However at the site of the primary prostatic cancer obstruction of the urinary outlet may occur despite the alteration of a patients hormone balance As a temporary measure it is occasionally feasible to insert an indwelling catheter The bladder may then be drained at intervals or permitted to drain continuously into a leg bag But this is usually unsatisfactory for patients do not tolerate indwelling catheters for protracted periods of time they usually develop secondary cystitis as a result of the presence of this foreign body More often it is necessary to provide a more adequate urinary outlet by means of a subtotal transurethral resection of the tumor When this is not technically feasible it may become necessary to create a permanent suprapubic cystostomy to maintain an adequate urinary flow In such instances it is possible by means of a bag similar to those used in ileal bladders to collect the urine and keep the patient dry Occasionally the reverse of this situation occurs When prostatic cancer involves the external sphincter of the urinary bladder the surgeon is faced with the control of urinary incontinence Although this does not present a problem of the magnitude created by urinary outlet obstruction it is nevertheless distressing to the patient Such a situation is usually controlled by the use of either a penile clamp or a device designed to collect the urine in a leg bag

Penile cancer can produce extremely distressing symptoms very similar to those noted in vulvar cancer A large ulcerated infected penile cancer is difficult to protect from the trauma of the patients daily

and gives the radiotherapist a better opportunity to treat the patient

EXTREMITIES —Malignant neoplasms that arise in the extremities and are no longer curable can produce many disagreeable symptoms particularly if the lesion becomes large enough to cause loss of function of the extremity or becomes ulcerated and infected It is often necessary to amputate these extremities to relieve symptoms and to simplify nursing care

Another interesting variant of this situation relates to vulvar cancer Patients with vulvar cancer have been encountered who were inoperable because the metastatic disease in the groin had become too extensive for the standard iliac and inguinal dissection The lesions had progressed to ulceration of the skin of the groin and had involved the femoral nerves producing much pain In one case a large draining sinus had developed from an infected lymph node containing cancer that originated beneath the inguinal ligament in another case the tumor had eroded the femoral artery and the major symptom was acute recurrent hemorrhage In both instances the use of the extremity had been denied the patient by the metastatic disease but the patient was in good general condition otherwise Both patients underwent hindquarter amputation and obtained considerable relief from their symptoms One survived but a few months, the other just over a year In both cases the palliation that was achieved justified the use of this mutilating type of procedure

only the clinical criteria should be used with no effort to study the internal mammary and supraclavicular lymph nodes by biopsy Because much can be said in favor of the control of the primary lesion in the breast as well as the disease in the axilla even though treatment may eventually fail these criteria may be crowded a little If clinical judgment should be in error *it seems better to err by giving the patient the* benefit of the operation For patients who are inoperable because of inflammatory carcinoma or because of clinically positive supraclavicular lymph nodes which are later proved by biopsy to contain tumor x ray therapy may be the treatment of choice The patients with patently disseminated disease (bone metastases) may be treated by alterations in hormone balance (see Chap IV) When bone metastases involve the vertebral column or a long bone in which a pathologic fracture might develop these local sites of metastases may be treated by x ray therapy

In cases of inoperable breast cancer, the local primary lesion may become quite large and ulcerated and result in pain or bleeding or both Patients of this type are often benefited by simple amputation of the breast, as part of the palliative treatment When the skin of the breast is involved, care must be taken to avoid transecting tumor in the course of the amputation Occasionally it is necessary to resect a large amount of skin along with the breast and actually to graft the thoracic cage Such surgery however provides much relief as far as the patient is concerned

compression type of laminectomy is necessary to avert or to correct a paraplegia resulting from such a fracture of a vertebral body Although this operation is usually classed as a neurosurgical procedure it should be included in the armamentarium of every well trained general surgeon since time is very important in the prevention of paraplegia

Pathologic fractures of the long bones may be given marked stability and the patient relieved of pain and deformity by the insertion of an intramedullary nail through the fracture True the passage of such a nail through a fracture of this type tends to disseminate the tumor along the course of the medullary canal but the stability given the fracture by such a nail outweighs the risk of such dissemination In addition it may be possible for the radiotherapist to treat the area involved Sometimes a marked amount of recalcification and bone deposition is noted following such treatment This type of operative procedure simplifies nursing care since large bulky plaster bandages and splints or cumbersome traction apparatus are not necessary in the care of the patient

Alteration of hormone balance —In breast cancer and cancer of the prostate it becomes necessary to alter the patient s hormone balance in an effort to effect a change of the biologic characteristics of certain of these tumors This is usually accomplished by the oral or parenteral administration of hormones In addition however hormone balance can be altered surgically by castration in both sexes and on occasion this is augmented by the surgical removal of the ad

Special Problems

Many special problems arise in the treatment of far advanced malignant disease Since the lives of many patients with malignant neoplasms can now be prolonged these problems arise with increasing frequency and require resolution A few of them will be discussed here

Anemia of hypersplenism —With the development of chemotherapeutic technics the hematologist is now able to prolong the lives of many of his patients suffering from the leukemias and lymphomas In certain cases the destruction of the elements of the blood formed by the spleen becomes a major problem Occasionally frequent transfusions become necessary to maintain the lives of patients in whom blood destruction is occurring at an ever increasing rate and with each transfusion the patient s reactions to the transfused blood become more acute It is possible in selected cases to decrease the need for frequent transfusions and provide much relief of their symptoms by surgical removal of the spleen To be sure these patients are poor surgical risks but the benefits to be obtained by splenectomy far outweigh the operative risk

Pathologic fractures —Surgical intervention is required when a pathologic fracture develops in a vertebral body and results in displacement of the vertebral alignment and compression of the spinal cord This may be further complicated by dislocation of the fracture with compression of the spinal cord A de

CHAPTER 6

Radiation Therapy in the Relief of Pain in Malignant Disease

IN PROPERLY selected patients who are suffering pain as a result of advanced malignancy, the radiotherapist may offer relief in a manner that is often quite spectacular Even when the pain is caused by metastases or direct extension from tumors which are ordinarily resistant to tolerable doses of radiation there may be complete relief if radiation is properly administered The radiation therapist must be aware of the limitations and dangers of his modality And rash promises to the patient must not be made nor should treatment be given where there is likelihood of doing more harm than good Usually treatment cannot be given when the overlying skin is already severely damaged and the effects of prior treatment on sensitive tissues such as bowel and kidney, must be considered The total body tolerance must also be remembered because when metastases are too numerous or the tumor bearing area too large, the amount of radiation that can be administered may be limited

renal glands These operative procedures are technically not difficult The important factors are the selection of patients for these procedures and the preparation for surgery and postoperative maintenance therapy

SUMMARY

Some of the surgical procedures available to the physician responsible for the care of the patient with advanced cancer have been discussed Even when incurable, cancer is a chronic disease requiring as it develops increasing efforts on the part of the physician to allay fear relieve pain and restore function The general surgeon s role in the treatment of the patient with advanced cancer is related not so much to the relief of pain as to the restoration of function Many situations that can be aided by general surgical procedures have not been covered, but from the discussion it is hoped that some general principles may be inferred to guide the physician in his approach to similar problems

RADIATION COMBINED WITH CHEMOTHERAPY AND SURGERY

There are numerous reports in the literature concerning the combination of chemotherapy and radiation therapy As yet there is no concrete evidence that there is more than an additive effect, but frequently there is good justification for the use of combined therapy When substances such as nitrogen mustard or the folic acid antagonists are used, relief of pain may be slow or incomplete In generalized disease the use of chemotherapy simultaneously with the application of radiation to the areas of most severe pain can produce more rapid and prolonged results

Rarely, however is radiation useful in combination with surgery It is unfortunately true that radiation is difficult to give following surgery and that satisfactory doses cannot usually be administered Time must elapse for adequate healing recovery of the patient, etc In most cases it is advisable to make a definite choice between the two modalities and use either one or the other Surgery for advanced cancer is usually quite radical and its sequel is usually diminished blood supply and increased fibrous tissue This situation prevents the use of adequate doses of radiation because of the danger of tissue breakdown In addition extensive surgery often requires the use of skin grafts which break down under the required dose of radiation

Surgery designed as an implement of radiation is an entirely different matter Actually the insertion of

to a dose which will accomplish relatively little

Many large volumes have been written on the role of radiation therapy in the management of malignancy This chapter deals with only one small facet of the problem and will accordingly be strictly confined to the control of pain The discussion of radium radioactive isotopes and supervoltage radiation is brief because while these sources of radiation are most important in the general field they have but limited application in the control of pain As a consequence the major emphasis is placed on the use of externally administered x rays in the ordinary range of voltage (200–250 kv) commonly but erroneously called deep x ray therapy"

X rays in this range are available to most patients within the limits of continental United States and for the purpose to be discussed here will be found in the hands of a diplomate of the American Board of Radiology within a 50 mile radius of the referring physician Modern transportation makes the daily trip for such treatment for the period of time usually required not too arduous Adequate hospital facilities are usually available where the distance is too great or the patient is too ill to tolerate travel

In general, the success of radiation therapy depends on the particular sensitivity of the malignancy to radiation Lymphosarcoma Hodgkins disease multiple myeloma and related reticuloendothelial diseases are very responsive to ionizing radiation Chondrosarcoma osteosarcoma and liposarcoma represent malignancies that are resistant to radiation

volved tissues Some otherwise well respected institutions advocate the use of relatively low voltage radiation in the range of 130–150 kv for rather deep seated lesions Such treatment demonstrates ignorance of physical principles and it not only is without much value in providing pain relief but is often detrimental because excessive damage to the skin frequently prevents later attempts to produce palliation in the same area

A wide range of radiation is now available Low voltage x ray machines with beryllium window tubes can operate at such levels that the radiation hardly penetrates the skin From this level the entire range is covered up to radiation produced by betatrons at 22 000 000 volts and by other instruments, such as synchrotrons, to much higher levels The radiation from radium falls at about the 1 000 000 volt level but the application of radium and its by products is quite a different matter because containers may be inserted within body cavities or into diseased tissues to deliver the radiation directly without traversing normal tissues

ARTIFICIAL RADIOACTIVITY

Since 1940 there has been a rapid development of a multitude of artificially produced radioactive elements For various reasons only a few of these have proved practical in the treatment of disease The three most important are radioactive phosphorus (P32) radioactive iodine (I131) and radioactive gold (Au198)

sources of radiation into cavities or tissues is a surgical procedure and the preceding statements are not intended as a criticism of such technics

PREVENTION OF PAIN

Before mentioning specific instances and giving some treatment details prevention of pain should be considered While in most cases extensions or metastases do not make themselves evident until they already produce pain there are occasions when experience will indicate that an inoperable and incurable malignancy is extending in such fashion that intractable pain will undoubtedly soon be present In such cases judiciously given palliative radiation can be of great value Radium supervoltage radiation or ordinary x rays may be used depending on the nature and site of the lesion

QUALITY OF RADIATION

The selection of the quality of radiation is the problem of the radiotherapist Often there is a choice but in general the quality of radiation will depend on the depth of the lesion to be treated Most pain producing lesions are deep seated and must be reached by radiation that is quite penetrating It must be emphasized that the important thing is *the amount of radiation which acts on the tumor* Radiation of the skin if not excessive is not important, nor is the dose to other organs or tissue but what is important, is to give the maximum possible dose needed while sparing unin

Certain cases of ovarian malignancy with widespread peritoneal implants producing ascitic fluid are benefited by the use of colloidal radioactive gold A solution of this substance, injected into the peritoneal cavity, spreads itself around fairly evenly and the results of the beta and gamma radiation often serve to decrease the production of ascites This type of treatment is usually reserved for patients who do not have appreciable masses in the abdomen since most of the effect comes from the very slightly penetrating beta particles Where masses are present treatment by external radiation is more successful

Numerous malignancies produce pleural effusion and radioactive gold is useful in these conditions Patients with effusion due to Hodgkin s disease lymphosarcoma and other radiosensitive diseases show the best results as might be expected less spectacular benefit is achieved in effusion due to metastatic cancer of the breast and similar malignancies Results similar to those of radioactive gold are obtained by the use of colloidal chromic radioactive phosphate There is little choice between the materials as regards effectiveness but from the standpoint of procurement, the rapid decay of radioactive gold is occasionally a disadvantage

Recent experimental work has indicated that adrenalectomy may be supplemented by removal of the hypophysis Because complete surgical ablation has been difficult and destruction by external radiation almost impossible, attempts have been made to eradicate the gland by implantation of radioactive sources

Radioactive phosphorus has found its greatest usefulness in the treatment of the chronic leukemias and polycythemia vera Because it is quickly accumulated in rapidly growing cells the greater portion of a dose collects in the bone marrow Here the beta particles or electrons, given off by the radioactive phosphorus as it decays destroy the abnormal cells with a consequent beneficial effect on the disease process It might be assumed from this that other rapidly growing abnormal tissues would be destroyed but this is usually not so because abnormal cell collections in locations other than the bone marrow find themselves in competition with the normal marrow for the radioactive phosphorus The usual result is a seriously damaged bone marrow and but little effect on the tumor

Radioactive iodine is rapidly collected in the thyroid gland where its primary effect is achieved by beta emission although it does produce some gamma radiation It is used in the treatment of hyperthyroid disease carcinoma of the thyroid and more recently to produce myxedema in certain types of heart disease In cancer of the thyroid, only certain types of tumors are affected—those whose structure resembles normal thyroid tissue and those giving some evidence of thyroid function Even when thyroid tumors have metastasized if iodine is concentrated by the metastases benefit may be obtained a few patients who had this condition and treatment are now living after more than five years without evidence of disease No benefit can be expected, however when little or no iodine is concentrated in the tumor

involves the sacral plexus In many patients with this type of disease, excellent relief of pain has resulted from a dose of as little as 2 000 r to the tumor In volvement of the brachial plexus by metastases of cancer of the breast or by upward extension of an apical lung tumor may frequently be very distressing Symptoms from such involvement can often be re lieved by the application of external radiation

While pain is only occasionally a phenomenon in edema, grossly swollen limbs can be a serious burden and the tense swollen skin can sometimes be quite distressing Local extension from carcinoma of the female generative organs often causes obstruction of the major pelvic veins and lymphatics, with result ant edema of one or both lower extremities When prior radiation to the pelvis has not been carried to extremes palliative measures may be carried out which will relieve these difficulties Radiation should be directed to the involved areas with carefully meas ured doses to the tumor and recognition of possible damage to the bowel and skin On the other hand a frequent sequel of combined surgery and postoperative radiation for carcinoma of the breast is edema of the arm This is most often caused by the scar tissue produced by both procedures not by extension or dissemination of malignant processes Further radi ation therapy in such cases is contraindicated since it will only serve to increase the difficulty

In similar fashion palliative radiation therapy for pelvic tumors may relieve bowel obstruction Often such treatment may be repeated even though the

Pellets of radio active yttrium (Y90) have been used for this purpose with some success Only time will allow full evaluation of this procedure

METASTATIC DISEASE AND LOCAL EXTENSION

Relief of pain caused by bone metastases is one of the most frequent requests made to a radiotherapist In general the results are good, in some instances, spectacular The results do not always depend on the radiosensitivity of the primary disease For example carcinoma of the breast is notably radioresistant, but properly administered x ray treatment will alleviate or even eliminate pain in many cases In the more sensitive tumors such as Hodgkin s disease and multiple myeloma relief can be even more striking but it must be pointed out that where pain is due solely to pressure on nerve roots by virtue of deformity little can be expected, for radiation cannot reconstitute for example, a totally compressed vertebral body At the other extreme painful metastases from hypernephroma give disappointing results However, no hard and fast rules can be made and an adequate trial of radiation of the proper quality to deliver a suitable dose to the tumor should be tried within the limits already mentioned

Not infrequently metastases or the local recurrence of a tumor involves nerve roots or nerve plexuses Here, again, surprising results are often seen even when the malignancy is known to be very radioresistant. Local recurrence of rectosigmoid carcinoma often

relief of obstruction may be very rapid when x ray is given to the mediastinum The type of cell influences the degree of response the best results occurring in the most anaplastic tumors

RADIATION SICKNESS

The great wealth of literature on the management of radiation sickness and the multitude of measures suggested for its control testify to the lack of knowl edge of its exact nature In the absence of laboratory evidence of toxicity a large portion of the condition must be considered psychogenic Patients have been observed who became ill before their first treatment and others have been seen who underwent the same radiation and never experienced a moment s illness Radiation is now so thoroughly publicized and talked about over the back fence that most patients will have an acquaintance who knows a neighbor or a friend who knows someone, who has 'had those x ray treat ments that make you sick at your stomach" Except in unusual cases the ordinary treatment does not make the patient sick Rarely is it necessary to suspend treat ment because of nausea and vomiting but even then the judgment of such suspension and the decision as to medication is best left to the radiation therapist

Modern radiation therapy combines a knowledge of radiology and physics and most of all, a wide experi ence in the art of the practice of medicine Patients referred for radiation therapy are best left in the therapist s hands until the contemplated job is done

malignancy is incurable The huge spleen with painful tense capsule seen in some leukemias may shrink following x ray Certain intracranial metastases particularly those from the sensitive tumors which produce headache diplopia and many other symptoms may be promptly and often permanently relieved by radiation In such cases adequate treatment will usually produce temporary loss of hair of which the patient should be warned Before undertaking treatment that will cause a disfigurement such as this the entire situation should be evaluated in terms of the total life expectancy of the patient No such treatment should be considered in patients who are near terminus due to other causes

OTHER COMPLICATIONS

A major symptom of Hodgkin s disease is pruritus Often this distressing condition will be present when no other evidence of the disease can be found The condition can frequently be relieved by irradiation with 250 kv x ray to the epigastric lymph nodes Since it is almost impossible to detect enlarged nodes in this area unless they are huge it is not surprising that this treatment is efficacious in widespread Hodgkin s disease

A frequent complication of inoperable carcinoma of the lung is compression of the superior vena cava with consequent dilatation of the vessels of the head and neck. While there is little evidence at present that radiation has curative possibilities in such tumors the

CHAPTER 7

Psychological Aspects of Pain in Terminal Malignancies

ALL PEOPLE experience pain and all people experience death Yet the emotional preparation for these experiences is as variable and various as the individuals who make up this world Some people accept pain and death with equanimity Others flee in terror

Intractable pain associated with cancer places the greatest stress on the emotional or psychological defense mechanisms that can be experienced in the field of medicine The management of pain in terminal malignancy may often be the greatest problem to the patient the family the hospital and the medical personnel in attendance There will be reciprocal stress in the patient his family and his doctor In this situation the physician is called on to accept and demonstrate the extent of his personal ability and therapeutic skill The reduction of pain depends on a constantly shifting relationship between the patient the family and the physician An attempt to define the psychological factors which may be present for each of these three

Conflicting recommendations after a course of management has been agreed upon can only undermine the patient's confidence and the old adage of "too many cooks spoil the broth" is too frequently true when the referring physician tries to manage the problems of radiation therapy

that of other sensations is accomplished by means of relatively simple and primitive neural systems which receive conduct and perceive impulses It is on this aspect of pain that the most active therapeutic measures have been devised

The reaction to pain on the other hand is a complex physiopsychological process which involves the highest cognitive or mental functions of the patient It represents the emotional and psychological expressions resulting from the perception of pain it is what the individual feels thinks and does about the pain he receives The pattern of reaction depends on what the sensation means to the individual in the light of *his past life's experiences and his attitude toward it* His attitude in turn depends on the mood emotional status the will the state of the various cerebral functional processes and the presence of anxiety and fear The reaction pattern which usually, but not always immediately, follows on the perception of pain assumes the form of the classic "fight, flight or withdrawal"

Pain associated with cancer is not one of unvarying suffering but differs in quality severity and duration depending on the mechanism producing it Pain will fall into the classic divisions of superficial deep and referred pain Rarely is there pain of central origin or psychogenic pain

Superficial or cutaneous pain is bright prickling and exhilarating in character and nature It can be accurately localized regardless of the site or origin The duration varies, and this may cause the patient to interpret the pain as being of variable quality Super

groups will be made here and suggestions for integration of the activities of all three groups will be given

Terminal and intractable pain occurs on the psychological background of these two factors (pain and death) which are most liable to produce disabling emotional patterns It is a cornerstone of modern dynamic psychiatry that the activity of the mental apparatus is in general directed by the organism toward the attainment of pleasure the avoidance of pain and the preservation of the individual All these are negated when the diagnosis of intractable pain resulting from a malignancy is known to the patient It is remarkable that more attention has not been given to the methods of handling the emotional responses derived therefrom

Because of the interlocking effect of pain and death on the psychological mechanisms of the individual it will be necessary in the following discussion to consider both of these facets and their interrelationship at all times It will be necessary to consider the effect on the patient, and also the psychological attitudes of the family the social environment and the doctor and other medical personnel who will be caring for the patient

GENERAL CONSIDERATIONS OF PAIN

Certain concepts are necessary in order to understand and relieve pain The basic factor involves two main processes the perception of impulses giving rise to the sensation of pain and the reaction and response to this perception The perception of pain like

of the individual, they are dependent on the intimate interrelationship between the perception of, and the reaction to pain

Intolerable or overwhelming pain is characterized by effects that are manifestations of what can be called an abnormal reaction to pain The patient performs continuous purposeless movements, rolls about, struggles and frequently cries and yells Observation or questioning reveals clouding of consciousness, and the patient s behavior is not influenced by his surroundings Moreover the pain is very diffusely perceived and vaguely localized

Severe pain is characterized by similar mental effects, only the patient is more aware of his surroundings The pain is vaguely localized because of the mental effects which prevent the individual from focusing his attention to such localizations The body is tensely fixed The patient groans winces and sighs during the height of the pain Stimulation of the special senses—by loud noises or bright lights, for example—causes distress Not infrequently the patient seeks sympathy seclusion and inactivity in an attempt to minimize the pain—the withdrawal reaction

Moderate pain is characterized by a fight or flight reaction which though momentary during the height of the pain, is so much in the foreground of total experience that primarily the pain is localized only roughly Subsequently however with a special effort, exact localization is possible

Mild pain is accurately localized and does not lead to any motor reaction It does not impair conscious

ficial pain may become an abnormal sensation usually taking the form of distressing cutaneous tenderness hyperalgesia, paresthesia and analgesia There may also be sensations of itching tickling and tingling

Deep pain has a dull aching quality It is extremely diffuse and poorly localized It is usually accompanied *by cutaneous tenderness hyperalgesia and hyperesthesia* located in parts remote from the stimulus There is frequently muscular rigidity or contraction which is associated with gland and smooth muscle effects and deep tenderness The localization and spread of deep pain depends on the intensity and duration of the stimulus An increase in intensity makes the pain less localizable and more widespread This pain may remain fairly localized to the involved organ or may be of a referred type

Perhaps the greatest difficulty encountered by the clinician is the estimation of the intensity of pain that the patient is experiencing This is because of the variability of individual reactions to pain making it difficult and at times hazardous to draw inferences regarding the intensity of such pain from observation of the patients

In the following discussion on clinically observable mental and physical effects of pain it is to be emphasized that this division is an artificial one used for the sake of convenience and clarity

Mental Effects of Pain

The effects of pain depend on the severity duration and quality and on the mentation attitude and mood

some cases as a result of sympathetic inhibition or parasympathetic stimulation there is a drop in blood pressure

RESPIRATORY SYSTEM —During severe pain the respiratory rate is, as a rule increased with a concomitant decrease in the volume, though it is not rare to observe an increase in the tidal exchange If the pain involves the chest wall or the heart the result is splinting of the chest, and breathing is principally abdominal in character If there is abdominal pain there is frequently a costal type of respiration

DIGESTIVE SYSTEM —Severe pain is frequently accompanied by nausea and sometimes by vomiting These effects are usually seen with a collapse type of pain reaction characterized by hypotension weak pulse sweating pallor and mental confusion and are most frequently associated with overwhelming pain In addition severe pain frequently decreases or completely inhibits gastrointestinal functions resulting in slowing of digestion and prolongation of the emptying time of the stomach

GENITOURINARY SYSTEM —Prolonged pain of intense degree causes a diminution in the patient s renal function apparently on a basis of vasoconstriction

AUTONOMIC NERVOUS SYSTEM —Superficial sharp pain seems to cause a sympathetic hyperactivity manifested by pallor pulsus alternans tachycardia, sweating goose flesh dilatation of the pupils and rise in blood pressure

All are manifestations of the fight or flight syndrome Overwhelming deep pain causes a withdrawal reaction

ness and it is experienced in the person s body but detached from the personality This pain comes near est to pure sensation It involves only the perceptive phase of pain

Physical Effects of Pain

Syncope —Aside from the mental effects already dis cussed there is one additional nervous system effect syncope which is primarily the result of overwhelming pain There are often symptoms of collapse which may progress to syncope This is probably secondary to sudden cerebral ischemia as the result of severe hypo tension due to hyperactivity of the central nervous system

Cardiovascular system —The general effect on the cardiovascular system is stimulation with superficial pain and inhibition with deep pain

Heart —Prolonged intense pain affects the heart and alters the T wave of the electrocardiograph Pain and fear have a definite effect on the heart as evidenced by the many reported cases of sudden death of pa tients with heart disease during a painful experience

Pulse rate —Pain alters the pulse rate The type of change depends on the intensity of pain Superficial pain causes a fight or flight reaction which is mani fested by tachycardia and consequent increase in the pulse rate whereas severe deep pain causes a slowing of the pulse and may even cause cardiac arrest

Blood pressure —Severe pain alters the blood pres sure It will frequently cause a rise in blood pressure in direct proportion to its intensity Conversely in

a foregone conclusion of an inevitable progression to subsequent death This chain of reasoning colors the patient's response to illness The extremes of emotional behavior are frequently seen and require great skill and knowledge on the part of the physician

The basic problem or factor in prolonged pain is the handling of fear This fear may rise from conscious or unconscious sources The conscious sources are fear of continuing pain or additional pain of mutilating surgery or other therapeutic procedures and of death There also may be unconscious fears which become activated by the dependent state in which the patient is placed by his illness and by the symbolic significance of the various organs involved in terms of the patient's past emotional experience There are also fears of separation from the family and of possible disintegration of the family unit and fears of economic chaos for the patient and for his family The usual responses to fear are disturbances of affectivity, or the feeling life of the patient These appear in proportion to the stability of the individual previous to the onset of his illness

Mental Reaction Patterns

In any illness, some depression and anxiety commonly occur and so a reactive depression is an obvious outcome of a serious illness Reactive depressions are those arising in response to obvious external causes which naturally might produce sadness An autonomous depression may also occur This type of

manifested by parasympathetic hyperactivity bradycardia drop in blood pressure, nausea vomiting sweating and alteration of gastrointestinal function

MUSCULOSKELETAL SYSTEM—Pain associated with deep somatic or visceral disease is accompanied by cutaneous tenderness hyperalgesia and hyperesthesia and muscular spasm Immobility causes skeletal muscle tension which may become a new source for noxious stimuli to aggravate the pain

METABOLISM—Pain is frequently accompanied by an increase in the metabolic rate and temperature of the individual This in turn increases the sensitivity to noxious stimuli and thus increases the severity of the pain Reflex irritability and oxygen demand are generally increased and in certain instances when pain is very severe these rise so greatly that a very large dose of opiate, or even a general anesthesia is required to lower them to normal

MENTAL OR PSYCHOLOGICAL FACTORS IN PAIN

The psychological effect of an illness on a patient is a function of the previously existing personality of the patient In general the more maladjusted the person was before the illness the more pathological will be his reaction to disease This is especially true in patients with malignancies With a malignancy there is a greater chance of pain suffering and fearful anticipation a greater chance of destruction or removal of organs and a greater chance of death A diagnosis of malignancy often carries with it in a patient s mind

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depression usually arises from unconscious guilt from interpersonal issues Guilt results from unconscious ambivalence and hostility with resentful and aggressive impulses directed toward persons or the object of undesired obligation or toward persons on whom one is dependent for security Hostile impulses originally directed toward other persons may become directed toward one s own self

Anxiety is a condition of heightened and often disruptive tension accompanied by a vague but often most disquieting feeling of prospective harm and distress Tension is a component of anxiety, but it is frequently recognized as a lesser form of anxiety, in that the patient has a continuing feeling of uneasiness restlessness dissatisfaction dread and discomforting expectancy

Fear is a response to an actual present danger It does not persist when the external danger which gives rise to it is eliminated Anxiety on the other hand with its persistent feeling of dread apprehension and impending disaster is a response to repressed dangerous impulses deep within the personality or to repressed feelings striving for consciousness It differs from fear in being referable not to specific objects or events but to an irrational dread of situations that covertly symbolize unconscious conflicts and impulses Anxiety and fear have much in common Both are responses to and signals of danger

The patient may also respond to fear by indifference or apathy, which would represent an excessive form of repression Apathy could be regarded as a protective

form of defensive reaction perhaps against painful perception

Panic may occur as a response to fear Panic is not merely a high degree of fear, but a fear based on pro longed tension with a sudden climax which is char acterized by fright extreme insecurity suspicious ness tendency to projection and disorganization In this situation the symptoms of hallucinations and de lusions of persecution are common The patient may react with self assertion and aggressiveness and may manifest autonomic signs of great fear yet remain immobile because he does not dare to move

All of these symptoms of mental disorder represent the patients attempt in the face of great difficulty to maintain an existence in the best possible way

Reactions to Illness

The meanings of a particular illness to a particular patient are based on conscious and unconscious sources When the patient is given a diagnosis he has to absorb the information in terms of the knowledge he has of it and in terms of the knowledge the doctor gives him The meaning of a diagnosis will therefore vary from patient to patient For the average person the meaning of an illness is determined first of all by other cases which he considers to be of the same disease whether really relevant or not In addition the meaning of the illness may be distorted by ideas arising from early childhood experiences which have emotional connotations and were simultaneous with

feeling states which are irreconcilable to the patient at the present time

The normal reaction to illness implies some anxiety and some depression, which very soon decreases to a concern approximately commensurate with the organic illness In other cases there may be an avoidance reaction in which the patient appears manifestly unperturbed sometimes denying his illness and shows overactivity and false gaiety This may be like a will o-the wisp and may turn into depression, anxiety or deliberate self harm by not following the physician s directions Other patients may show a reactive depression with some prolonged emotional retardation and hypochondriasis A more pathological response to illness would be a channeling of all previously existing anxiety into a new groove of concern This may cause the patient to give up many of his diffuse neurotic disturbances and cause him to appear more tractable at the moment

All severe incapacitating illnesses increase the need to be loved and cared for Enforced inactivity, in turn adds to the wish to return to a dependent more or less childlike status Such an unconscious desire may express itself in rationalizations, inappropriate symptoms and demandingness Fears of possible harm by lack of care stand in the center of such behavior

Reactions to Malignancy

In an illness due to a malignancy or suspected malignancy the gamut of emotion may run from the delu

sion of having cancer to a complete denial of the disease by those already afflicted All kinds of irrational attitudes come to the fore These emotional attitudes are dependent on the patient s attitude toward danger and destruction they represent his individual methods for handling his fears arising from conscious and unconscious sources It is the meaning of "malignancy or "cancer" which determines the emotional reaction There may often be a magic attitude toward the diagnosis of cancer as if it were a death sentence, and this becomes the focal point of the psychodynamics of the patient

Images that patients may have of malignancies range from those of having a body riddled with holes to an attribution of living invading "things, or anthropomorphization of the invading cells

There is, in all cases a subjective meaning of the particular malignancy To some people for instance an ulcer represents a hole in the body and this idea upsets them Much of the emotional charge about this hole may be derived from infantile notions of the differences between boys and girls and the feeling that girls are different sexually because they have somehow been damaged The concept of an ulcer as a hole then revives such early fears and derives much of its irrational horror from this source On the other hand some patients visualize their malignancies as growths Even limited psychiatric investigation sometimes reveals that this growth inside the body is equated with another type of growth (a pregnancy) A little child cannot understand the facts of life and

unconsciously the ideas and fears of childhood live on to distort our grown up rational understanding Such notions often add further terrors to the realism of malignancy

Patients may conceive of themselves as being help less and impotent against the cancer enemy they feel like passive and helpless children Doom stalks them in the form of worse imaginings The emotional situ ation of the cancer patient has become more difficult because of a general artificial cancerophobia as the result of increased publicity about malignancies Cam paigns aiming to enlighten the public about malignant growths are often used by neurotically inclined indi viduals to increase their fear Some people definitely do not want to know the truth about themselves They look upon every examination for cancer as though they were already certain of a fatal verdict It has been observed that once the diagnosis of cancer has been established the patient suddenly becomes much worse The combination of the tumor plus the fear or the illusion that the diagnosis means a fatal verdict brings the patient to a state of melancholy and compulsive preoccupation with his symptoms setting off a vicious cycle that brings him sooner to the end of his resist ance He may make life intolerable for himself and his family

Because there is always a possibility that there may be relief, the dictum of treating anxiety whenever it is encountered and wherever it occurs should be ad hered to It is the task of the doctor to interpret such fears from some of the random remarks that the pa

tient makes in order to cope with the realistic problem of the basic illness

Reactions to Immediate Danger of Loss of Life

At the time of an actual immediate danger of loss of life there is frequently some alteration of brain function Such changes often lower the level of con sciousness and impair complex intellectual functions and this seems to facilitate a delay in the patient s recognition of the serious nature of his condition The patient slowly comes to realize how sick he is The changes in brain function seem to make it easier for him to restrict his awareness, to decrease pain per ception and to perceive only those elements in the environment which he wants to perceive, and to delay recognition of the threat to life

The defensive psychological reactions appearing in an attempt to handle the threat of death generally are of three types (*a*) processes which tend to make the patient feel that his life is really not in danger (*b*) processes in which the patient seems to feel that, even though his life is in imminent danger it does not really matter—that is he is not concerned by his im pending death and (*c*) processes which tend to make the patient feel that, even though his life is in danger now it will not remain in danger—that there is some thing that can be done to correct this situation

A given patient is not limited to any one of these defensive responses but may show different ones at different times These responses may be aimed at com

bating either the illness itself or the fear derived from the illness They involve not only conscious thought and voluntary action but to a large extent automatic nonconscious processes

The reaction of purposeful alteration is manifest in a denial of illness The patient simply does not recognize that he is seriously ill although he is capable of recognizing many other equally complex facts of his environment In addition, some patients reject not only recognition of the illness but most or all of their current and environmental situation as well They appear to be largely out of contact with reality

Another reaction is that in which the patient recog*nizes the nature of a current situation and concludes* that he is going to die This type of patient is frequently observed to be the seriously ill patient—tired weak and in pain—who comes to feel that what happens to him does not really matter At the moment it may seem to him that to die is only to rest quietly and escape from suffering A similar instance of the acceptance and preparation for imminent death is that in which religious feelings play an important part Here the individual in a time of emergency mobilizes powerful feelings of God s protection While this is usually an emergency defense in that the patient feels that God will probably protect his life and let him avoid death there is also the feeling that God will take care of him in case he should die Thus he is prepared either way for whatever may happen

Another type of reaction is that in which the patient feels that even though his life is in danger now it

will not remain in danger He seems to be in danger of being overwhelmed by emotionally painful stimuli and he handles the problem within himself by thinking about the situation only when he must do so and even then, allowing himself to have little or no feeling about it He often seems indifferent, unemotional and apathetic

Virtually all patients at some time or another clearly demonstrate the type of process in which a conscious effort is made to avoid thinking of an unpleasant experience

These defensive reactions make it possible for the individual to avoid overwhelming disintegrative panic Under optimal conditions they facilitate not only relief of fear but preservation of life and recovery from illness as well In extreme forms however, they may be biologically maladaptive since the individual sometimes abandons long range life preserving functions in favor of momentary relief from discomfort

Individual Reactions to Pain and Removal of Organs

As part of the therapeutic process for alleviation of chronic pain in malignancy various organs may be removed and reaction patterns may occur as a result of an injury to or destruction of a part of the body which has special or specific significance for the individual alone The reactions will vary with the part of the body and the type of function affected This is particularly true relative to areas of the body which

have a sexual connotation For instance breast cancer obviously afflicts an organ for which a woman bears much pride as an erotogenic zone and which is particularly invested with meaning from an emotional standpoint Amputation of a breast may involve a total change of the patient s image of herself as a woman It definitely alters her role as a sexual object to her husband and it alters her world somewhat

Patients with a malignancy of the gastrointestinal tract are exposed to all the deprivations of diet that are current in the treatment of these diseases And patients with anal difficulties have to face uncleanliness, which may have been taboo ever since early childhood and which may deeply upset the individual

The idea of a growth inside the body may revive irrational childhood fears of pregnancy (that is a form of internal growth) and notions of a bleeding opening in the body may again arouse primitive concepts of bodily mutilation

Cancers of the larynx ear nose and throat are particularly invested with symbolic unconscious meaning derived from early childhood fantasies

In pulmonary cancer early anxiety may occur with a *vague feeling of respiratory distress or embarrassment*—as though breathing was not safe anymore

Along with the cachexia that occurs as a part of illness, infantilism in the patient frequently appears Hunger and fear of death break through the ordinary control of emotions

Thus to each individual each part of the body has a different meaning and it is just this individualized

meaning that accounts for the different reactions to the various pains and procedures in the therapy of cancer

PATIENT-FAMILY REACTIONS

The chronic illness and persistent pain in terminal carcinoma may place strong and excessive stresses upon the family s emotional ties with the patient The family members who have strong emotional attach ments to start with are most likely to take the patient s fears pains and fate personally Panic often strikes them Whatever guilt feelings they may have toward the patient emerge to plague them They wish they had been pleasant and good to the patient and are now doubly struck by every injustice they feel they might have done Hypochondriasis in members of the family of the one afflicted with a malignancy is often the result of unconscious thoughts such as I have been so unkind to him that I too deserve to be fatally ill" An alert physician has to understand these feelings and other ramifications of the emotional identification of the family with the patient

When the illness and pain are particularly pro longed two reactions may occur in a family Initially there is the strong identification with death destruction and pain Then as time passes the identification may become so painful to the members of the family that they will erect psychologic defenses in order to protect themselves The most common form of reaction is a rejection of the need for prolonged identification with the patient This takes the form of decreasing interest

and mild isolation of the patient, and visits to the patient may become briefer and less frequent Despite the use of this device however the relatives may feel guilty because of actual or implied neglect, which will in turn generate feelings of hostility toward the sick relative Such a reaction depends on the duration of the illness and the ability of the patient to communicate his anxiety fears and pain to the various members of the family

If the patient is maintained at home many frustrations and physical demands may be imposed on the family by the advanced illness There may develop extreme weakness incontinence and bad odors The pressure of caring for the individual under these circumstances is likely to arouse a resentment and in turn guilt feelings on the part of those who have to do the nursing

The duration of the illness may also involve financial stress for the family Chronic illness is expensive and after the initial period of personal identification with the patient, the family may soon come to feel that a quick death would be of benefit to the patient and would indirectly relieve the financial strain imposed on the family Within the family group there may be rivalry and conscious or unconscious competition for the patient s estate While these matters are not discussed with the patient they may be discussed at some length among the peripheral members of the patient s family group These persons in turn may generate resentment and hostility because of the decrease of the estate by the prolonged illness The frequent bed

side visitors may therefore be operating on a compassion made up of mixed motivations

There has been some tendency to keep the diagnosis of a malignancy a secret from the patient but to share it with a family member This produces many difficulties A daughter who has been told secretly that her mother suffers from cancer herself suffers a great deal of anxiety and probably communicates that fear and concern whether she wishes to or not. It is doubted that a policy of secrecy succeeds very often

The doctor has the task of deciding what type of approach to use with the personality of each patient or relative in mind In the vast majority of situations probably a rational discussion of impending problems with the patient and family will be most useful

Patient Physician Reactions

The fears and anxiety of the patient with carcinoma and pain will be influenced by the attitude or advice of his physician Thoughtless and unfeeling statements may precipitate excessive fear and invalidism Of necessity contact with any patient arouses feelings in the doctor just as the doctor arouses feelings in the patient Working with a patient suffering from a malignancy causes special problems for the physician First of all the patient with a malignancy is most likely to engender anxiety concerning death even in the doctor And at the same time this type of patient constitutes a serious threat or frustration to medical ambition As a result a doctor may react more emotionally and

less objectively than in any other area of medical practice He may at times be carried away to make more optimistic statements than are warranted and at other times his deep concern may make him more pessimistic than is necessary

As a result of the feeling of frustration in his wish to help the doctor may have moments of annoyance with the patient He may even feel almost inclined to want to avoid this type of patient

As in all patient physician contacts, the patient perceives the finest nuances of the doctors attitude unconsciously if not consciously The patient of course views himself as a sufferer and expects help from the doctor His attitude is frequently like that of a child toward a parent At the same time the childhood attitudes which the patient ordinarily keeps under control but which appear more readily during a period of dependency and illness may lie behind his desires and demands on the physician and his attention These unreasonable attitudes will need to be recognized by the physician Also to maintain a patients relatively un neurotic attitude toward his illness it is necessary that the doctor be aware of inappropriate emotions aroused in himself by the patient Once the physician is aware of his own problems he can exclude them or at least control them so as to cause minimal interference in handling the therapeutic program for the patient

PATIENT CULTURE REACTIONS

Frequently cultural patterns dictate how the individual should bear pain American culture emphasizes

independence and personal accomplishment Excessive display of emotional reactions regardless of the cause, is frowned on In addition there is a lack of sanctioned outlets for the satisfaction of passive dependent needs of the individual The American family structure, in an early portion of the individual s life, has intense emotional relationships among all members However since our culture emphasizes independent and personal accomplishment, the child s close attachment to the mother must be resolved When the time comes for the individual to be separated from the family unit, latent deep seated dependent longings may emerge and the psychologic defense against this may precipitate an anxiety as these feelings come into the pa tient s awareness Illness pain and fear of death tend to activate the dependent longings Conflict can easily arise since it may be very difficult for the individual to satisfy his need for these passive dependent needs and his previous concept of the necessity for a com petitive constructive individuality Our culture pro vides few defenses for this type of stress beyond a suppression of the need If the individual s defenses break down he may feel angry toward himself and toward the members of his family The patient must frequently admit death and pain as a part of nature beyond his control, but he can try to, or does, sup press his thoughts and emotions about these subjects The demands of the social environment, excessive competitiveness sexual repressions and contradictory codes bring individual frustrations and dilemmas and engender psychic conflicts Social factors and

standards help to shape the adaptive effort of each individual but when operating with biological and psychological influences, may be partly responsible for the formation of personalities that eventually come to neurosis and psychosis

MODIFICATION OF THE PAIN REACTION PATTERN BY PSYCHOLOGICAL SUPPORT

In no other disease is the patient s need for moral, or psychological support so great as in intractable pain associated with cancer This assistance takes the form of not the usual psychotherapeutic procedure, but sincere sympathy understanding kindness and moral support by the physician The aim of psychological support is to reduce tension fears and anxieties which produce hyperactivity of the mechanism for reception and reaction to pain In such psychological support one begins at the base of the process which transforms "body to "mind" This is essentially an investigation of psychosomatic relationships based on the personal social and cultural experiences of the individual and on the individual physiology and psychology

To begin with the treatment of a patient will involve an investigation of his general life situation at the time the illness arose and of the sequence of events since that time It is assumed, of course that a thorough history and physical examination have been made and that laboratory procedures have been completed as indicated, in order to establish the diagnosis

The general physician is in a particularly advanta geous position, since he may have known the patient for some time, may know his attitudes toward illness pain and death and may have intimate knowledge of the family relationships

It is perhaps easiest for the physician to proceed from physiological to psychological investigation and explanation to the patient All too frequently, the pa tient has conscious fears which are exaggerated by obscure medical terminology and incomplete explana tions The simplest thing the physician can do is to clarify in simple terms the definition of the illness that has been diagnosed This in turn will decrease the anxiety that always accompanies something which one does not understand It may be necessary to institute a mild program of education regarding the physiology and anatomy of the body and the organs which are now affected It is certainly wise to give a tentative explanation of the various therapeutic procedures which the patient may anticipate the duration of the procedures and their purpose Such explanation must be given in simple terms which the patient can under stand or relate to his past experience The rationale of the disease process and the healing phases which may occur should also be discussed If pain is extreme the physician may be more specific in telling the pa tient details or procedures to avoid increasing pain and in so doing he involves the patient in an active portion of the therapeutic program and allows him to share some of the responsibility in securing the de- sired results in treatment A single explanation may

not suffice Frequently the patient physician tolerance limit is approached by the patient's demands for repeated and detailed explanation There is no point in showing impatience, irritability or annoyance at the time of these repeated demands A simple way to avoid them is to ask the patient to define what he remembers of his own illness or to verbalize his illness in his own words The physician should particularly avoid an attitude of despair or defeat The patient is quick to sense this or a lack of interest and he may be forced into emotional patterns which defeat the eventual purpose of treatment The physician should do all he can to give the patient a sense of confidence and security based on the conviction that everything will be done to relieve his suffering and that his problem is not meaningful to him alone

The intimate relationship of the patient and physician makes it possible to explore many of the unconscious sources of fear and anxiety which the patient has The patient frequently regards his doctor as a sort of confessor friend sympathetic and understanding listener and often a useful visitor Particularly in respect to a malignancy in an organ which has a sexual connotation or pain arising from such a structure the doctor will need to inquire into the meaning of this condition to the patient. Such inquiry does not require extensive psychiatric knowledge but it is not unreasonable to assume that the physician will be aware, working wise that destruction or removal of organs which are basic to the concept of masculinity or femininity will be emotionally traumatic The ex

planation usually required of the physician should indicate a lack of change in the basic body image If necessary, a discussion of childhood experience with various organ diseases can be undertaken This can be done simply by asking the patient, "Whom have you known with illness of this type before?" or, "What do you remember about illnesses of this type?"

A patient with malignant disease who is suffering pain more or less constantly soon guesses the progno sis despite the efforts made to conceal his doom He may ask questions concerning the possibility of death or may indicate that he expects death If this subject is brought up by the patient, it should be met with understanding and consideration A matter of fact ex planation of the possibilities of death may be given together with reassurance that no matter how severe the illness there always is a possibility of arrest of pain and recovery Depending on the experience of the physician and the patient s own religious attitudes the properly oriented priest, minister or rabbi may be used effectively in sharing the preparation for death In general, a matter of fact sympathetic listening at titude is probably the best approach to this problem Certainly there is little the physician can do to alter the fear of death

An additional aid to the doctor may lie in the tech nic of handling the complaints regardless of how badly they are expressed While "a stiff upper lip" approach may be used at times on the other hand it may be necessary to be permissive and to express a willingness to listen to the patient s bitterest complaints concern

ing his pain Even a momentary description of the severity of the pain in whatever terms the patient has available may relieve sufficient tension so that he is able to carry on in a manner most suitable to his needs when persons other than his physician are present

When the patient comes to realize the presence of malignancy and chronic pain he may need to put his personal house in order The physician can recommend that a business like review of the personal affairs of the patient be made in the same manner as if he were entirely well

The family of the patient may also require a good deal of psychological support The members of the family will certainly seek out the physician to express their uncertainties and fears concerning the patient It will be necessary to answer questions of anatomy and physiology but this should be done as briefly and simply as possible This is probably most efficiently done by giving an explanation to a single stable individual who can then communicate with the other members of the family Of course this procedure carries a risk of misinterpretation but it is advantageous in that it lessens the time required to talk to each individual alone One of the points that might be emphasized is that everything possible is being done for the patient It is wise to avoid specific predictions as to the time of death or the duration of the illness A physician who does state a specific time may be put in an extremely embarrassing position by a complete recovery

In relation to visiting with the patient, the physician

can recommend that there be no exaggeration of interpersonal relationships with the patient The patient is, after all still a member of the family group and activities of the family will still be of interest and will aid the patient in avoiding a sense of separation and hopelessness in regard to his illness It is equally important that an overconcern or overprotectiveness not be demonstrated by members of the family, the patient will read enough into their minimal changes in attitude without a questionable overconcern on their part Other important factors are to assure accessibility to at least one responsible member of the family and to assure the family that they will be notified of any medical changes in the patient s condition A responsible and stable member of the family may be encouraged to discuss the necessary reorganization of family relationships and personal and financial responsibility which will be necessary if and when the patient dies

MODIFICATION OF THE PAIN REACTION PATTERN BY HYPNOSIS

As has been repeatedly emphasized so far in this chapter there is a great emotional problem in each patient with cancer and with severe pain If the emotional tension in the patient can be channeled away from a neurotic exaggeration of fear and self pity to a more realistic and constructive point of view this energy will be available to support the patient during therapy When therapy is completed the patient should have a more serene and confident attitude until death

With such an approach there will be less pain less disturbance in bodily function and a reduction in the degree of dread that surrounds the subject of cancer

Hypnosis may be used to suppress symptoms or through application of analytical principles to express emotionally charged ideas In some patients hypnosis allows a control over the subconscious mind, and the mind can thereby be maneuvered to aid the cancer patient in his struggle for survival Hypnosis offers difficult problems and most of the responsibility rests on the physician who undertakes this type of therapy

Historically the physician has ample precedent for hypnosis since it probably is older than medicine It certainly was used in Egypt and Aesculapius was said to have been able to relieve pain by stroking his hands on the patient s brow The use of hypnosis has had repeated ups and downs and is now receiving new interest with a gradual diminution in both professional and popular resistance to hypnosis

Hypnosis may be defined as an artificially induced state characterized by heightened suggestibility In hypnosis a special integrative interaction of the organ ism with its environment results in certain sensory motor and memory changes The hypnotic situation is a special type of interpersonal relationship and phenonema observed in hypnosis are the result of the interaction between the hypnotist and the subject The behavior of the hypnotized individual represents a psychosomatic response to the cues of the operator within the framework of this relationship

At present there is no physiological or psychological theory available which accounts satisfactorily for all the phenonema encountered in hypnotic states Also practically nothing is known concerning the reasons for the individual differences in hypnotizability or for the relationship of hypnosis to various related states such as barbiturate narcosis and drug intoxication The actual hypnotic technics should be learned under expert guidance Such technics are taught in most of the larger centers of psychological training and in many of the larger psychiatric hospitals Hypnosis is a process which when learned will be of use in other areas besides the control of cancer pain

In general, it has been noted that pain anxiety and organ dysfunction in a patient with cancer can be influenced by hypnotherapy The results are however proportional to the depth of the trance and the intensity of the program of therapy Before the hypnotic process is begun it is essential that the hypnotist have a detailed history of the patient, with special attention to psychosomatic factors previous impressions regarding hypnosis and the present social environment of the patient. It is certainly best that the subject of hypnosis be directly discussed with the patient and that the procedure be done with his permission

In all circumstances the depth of hypnosis is the deciding factor in its success For practical purposes there are three stages a light, a medium and a deep trance In a *light trance* the patient recognizes some influence but doubts that he was hypnotized In a *medium trance* the patient is sure he was hypnotized

but he can recall freely all the events that occured In a *deep trance* the subject realizes that he was hypnotized but his recall of the trance period is under the control to some extent of the hypnologists sug gestions If after about three one hour periods of in tensive work, a patient reaches only the light trance he cannot be helped by hypnosis The patients who go into a medium trance can be helped, but the more severe the organic pain the more ephemeral will be the hypnotic control Those who reach the deep or somnambulistic trance can be helped Unfortunately such persons are rare constituting only 10–20 per cent of the population Extensive disease, a distraught mind pain and the fear of death make induction of hypnosis more difficult than in normal persons Thus it seems that the most difficult thing to control under hypnosis is the very function that the physician most wants to affect

The hypnologist is an important factor in this prob lem, for hypnosis is a transference and a countertrans ference relationship just as is psychoanalysis In hyp nosis the interplay is not well understood by either party and is not well handled Here the differences in sex age race and social situation of the patient and the hypnologist become acutely important and may if these factors are diverse militate against success

The main disadvantages of this form of therapy are the few good subjects the large amount of time required and the necessity for an experienced and well trained hypnologist to govern each case The pos

sible deleterious effect on the health of the hypnolog ist and the long period of time required for one pa tient, between onset of symptoms and death thus limits the number of patients a single therapist can manage Then too public resistance to hypnosis persists

The advantages of hypnotherapy for patients who enter a deep trance are numerous Drug requirements are lessened pain is relieved organ dysfunction can be corrected as much as is possible and depression anxiety and fear are minimized Life is prolonged and death is approached as is a night s sleep

Prefrontal lobotomy interferes with the induction of the hypnotic state in proportion to the decreased abil ity of the patient to concentrate so that results appear to differ from the hypnotic state *Narcohypnosis* helps to counteract superficial resistance but does not seem to aid otherwise in obtaining true hypnotic depth It does not eliminate all resistance

Efforts should be extended to learn what hypnosis is and how it alters physiological function When these fundamentals are understood, its advantages will have a wider and more satisfactory application Hypnotic experience has indicated that there may be a cancer personality Intensive study shows that the patient with cancer is either an inhibited individual with repressed anger hatred or jealousy or a good person consumed with self pity

Hypnotism is not to be considered lightly Its use must be restricted and it is safest in the hands of a competent psychiatrist who has had a particular in-

terest and experience in it Other specialists and general physicians should use it only after adequate training and then only when other available methods are inadequate The use of hypnotism can be compared to the performance of a difficult operation Anyone can cut the skin many can remove an appendix but few should remove a stomach a pancreas or a lung The same is true of hypnosis Anyone can learn to induce it some can get therapeutic results, but only those with experience and training should attempt to cut out pieces of the mind

CONCLUSION

The psychological problem of pain in terminal malignancy is a problem of the total relationship of the individual the family the physician and society The attitudes which the patient has will be a product of past experience both conscious and unconscious the kind and degree of disease which he now has the duration and severity of his pain and his personal attitude and preparations for death The reaction to pain will be based on reducing the unknown Attempts should be made to reduce fear and anxiety and to simplify personal family and spiritual relationships The ultimate substance of treatment should be that the physician is doing all he can to give the patient confidence and a sense of security based on the conviction that all is being done to relieve the suffering and that all of his needs will be met within the realm of reasonable possibility

Index

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